The New England
Journal of Medicine

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Volume 255 DECEMBER 27, 1956 Number 26

ANEMIA ASSOCIATED WITH VITAMIN D INTOXICATION*

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THE clinical picture of vitamin D intoxication has been described in detail by a number of observers.[1,2] Particular emphasis has been given to renal failure and metastatic calcification, with attention also to the laboratory abnormalities present. The importance of establishing the diagnosis, in view of the frequent reversibility of the condition with proper therapy, has also been stressed. This report concerns 4 patients who were seen primarily because of unexplained anemias that were refractory to the usual therapeutic agents and for which there was no apparent etiology. When the specific history of vitamin D intake was obtained the entire clinical problem was resolved by means of the appropriate studies.

The 4 patients described were referred by other physicians as diagnostic hematologic problems. Two were hospitalized when first seen, and in the 2 others the diagnosis was strongly suspected on examination in the physician's office. This clinical syndrome has been most instructive to us, and it was thought that a description of these patients and the problems that they presented was worth a detailed report. An attempt has been made to study the type of anemia that was present (Table 1) and to describe the significant clinical and laboratory data (Tables 2 and 3).

CASE REPORT

CASE 1. F. R., a 56-year-old bank worker, was admitted to the Albany Hospital on October 6, 1952, with the major complaint of weakness and headache. He felt well until November, 1951, when these persistent symptoms had begun. He consulted his family doctor and was found to be anemic. He was admitted to another hospital, but no explanation was found for his anemia although skull changes consistent with Paget's disease were observed. Urinary frequency and occasional nocturia had been present for several months. Liver and iron therapy was given orally during 1952.

Physical examination revealed an anxious, restless, pale man who appeared chronically ill. The frontal bones were prominent. The hue of the skin was somewhat gray. The blood pressure was 100/60. Positive findings were a small calcium deposit in the left cornea, firm liver palpated 2 fingerbreadths below the right costal margin and an enlarged prostate.

Examination of the blood showed a hemoglobin of 9.0 gm. per 100 ml., a red-cell count of 3,110,000, a hematocrit of 28 per cent, a white-cell count of 7300, with a normal differential, and reticulocytes of 1.2 per cent. Urinalysis revealed a specific gravity of 1.007, but was otherwise negative. The blood sugar was 108 mg., the nonprotein nitrogen 51 mg., the alkaline phosphatase 0.8 units, the albumin 3.2 gm., and the globulin 2.6 gm. per 100 ml. An x-ray film of the chest was normal; an electrocardiogram was reported as showing nonspecific ST-segment and T-wave changes. Stool tests for occult blood were repeatedly negative, as were barium-enema and upper gastrointestinal examinations. At this point the patient was seen by the hematologic service because of increased hemosiderin observed in a bone-marrow aspirate, which was done because of the unexplained anemia. The diagnosis of hemochromatosis was suspected. Further questioning disclosed that he had taken "Darthronol" (50,000 units of vitamin D), 3 to 6 capsules daily, for 6 years, originally started because of "asthma." Additional laboratory studies were then ordered.

Repeated nonprotein-nitrogen values were 64 and 91 mg., and the creatinine 4.5 and 5.8 mg. per 100 ml. The calcium was 7.1 milliequiv., and the inorganic phosphorus 1.2 milliequiv. per liter. A urinary Sulkowitch test was +++. Phenolsulfonphthalein excretion was 10 per cent in 2 hours. Repeated determinations of the specific gravities were not over 1.007. A Congo-red test was negative. Intravenous pyelograms showed poor excretion of dye but no calcification. A Fishberg concentration test on the urine yielded a maximum specific gravity of 1.007. Urea clearance was 16.4 per cent. Bone-marrow examination was unremarkable except for a marked increase in hemosiderin. Dental films showed loss of definition of the lamina dura. On October 29 the calcium was 5.8 milliequiv., and the inorganic phosphate 2.3 milliequiv. per liter.

The diagnosis of vitamin D intoxication was thought to be substantiated, and this was confirmed by endocrinologic consultation. It was believed that the rising phosphorus was very much against the diagnosis of parathyroid tumor. The patient was discharged on November 2, on a high-fluid, low-calcium diet.

He was readmitted to the hospital for evaluation on November 30. He had noticed a steady, marked improvement in well-being and decreased fatigability. The hemoglobin was 9.5 gm. per 100 ml., the red-cell count 3,100,000, and the hematocrit 30 per cent. The nonprotein nitrogen was 67 mg., and the creatinine 4.5 mg. per 100 ml.; the calcium was 5.8 milliequiv., and the inorganic phosphorus 2.6 milliequiv. per liter, and the alkaline phosphatase 1.1 units. A Fishberg concentration test showed a maximum specific gravity of 1.010. Urea clearance was 20.3 per cent; an intravenous phenolsulfonphthalein test revealed 7.6 per cent excretion in 2 hours. Liver biopsy demonstrated an increase in hemosiderin but no fibrosis was observed.

The patient was last seen on December 16, 1953, when the symptoms were strikingly improved. The easy fatigue and polyuria were absent. Examination of the blood showed a hemoglobin of 10.6 gm. per 100 ml., a red-cell count of 3,440,000 and a hematocrit of 32.5 per cent.

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This patient had been followed for almost a year with an undiagnosed anemia refractory to therapy. Marked symptomatic improvement occurred with proper therapy for vitamin D intoxication. However, severe renal disease still persists and demonstrates the problem of irreversibility of this disease with prolonged intake of the vitamin. The anemia has not been completely cured and seems to parallel the renal insufficiency.

the alkaline phosphatase 0.6 units, and the serum protein 5.1 gm. per 100 ml. (albumin of 3.4 gm.). The stools were negative for occult blood. An x-ray film of the chest was normal; a plain film of the abdomen showed no renal calcification.

The history and chemical findings were believed to establish the diagnosis of vitamin D intoxication with anemia due to this abnormality. The patient was then treated with a low-calcium diet and a high-fluid intake. After 3 weeks of treatment she was discharged. Symptomatically, she showed definite improvement. The hemoglobin had risen to 10.5 gm. per 100 ml., and the hematocrit to 31 per cent. The non-

TABLE 1. *Hematologic Aspects of Vitamin D Intoxication.*

SUBJECT	HEMOGLOBIN	RED-CELL COUNT	HEMATOCRIT	WHITE-CELL COUNT	RETICULOCYTES	BONE-MARROW EXAMINATION	MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION*	MEAN CORPUSCULAR VOLUME†	NONPROTEIN NITROGEN	RESULTS OF FOLLOW-UP STUDY
	gm./100 ml.	*X10⁶*	*%*	*X10³*	*%*		*%*	*cu. microns*	*mg./100 ml.*	
Case 1	9.0	3.11	28	7.3	1.2	Hypercellular; increase in eosinophils & granulocytes; increased iron.	32	90	64.0	At 14 mo. hemoglobin 10.6 gm. per 100 ml. & hematocrit 32.5%
Case 2	9.8	3.01	29	7.25	1.1	Normal	31	96	60.0	At 7 mo. hemoglobin 12.5 gm. per 100 ml., hematocrit 41% & nonprotein nitrogen 41 mg. per 100 ml.
Case 3	8.3	3.3		7.5	—	Moderate hypoplasia of erythrocytic series			103.0	——
Case 4	10.75	4.01	32.5	8.5	1.4	Normal	33	80	22.6‡	At 3 mo. hemoglobin 12.3 gm. per 100 ml., hematocrit 38% & nonprotein nitrogen 36 mg. per 100 ml.

*Normal, 32-36%.
†Normal, 82-92 cubic microns.
‡Blood urea nitrogen.

CASE 2. S.L., a 52-year-old single woman, a clerical worker, was studied on November 3, 1953, because of an unexplained anemia. The history revealed that she had been treated for arthritis for 10 years. She had received intermittent injections of vitamin D approximately once a week and 1 or 2 "Darthronol" capsules daily (50,000 to 100,000 units of vitamin D) for 3 years. She had complained of insomnia and some pruritus for about 8 months. Nocturia (3 or 4 times) accompanied the insomnia whereas only mild frequency occurred during the day. In September she visited her physician, who found an anemia and prescribed liver, iron and vitamin B_{12}. This therapy had no effect on the blood count. The past history revealed a hysterectomy in 1951, when the blood values were normal. In 1950 a breast biopsy was done for a benign tumor, and hematologic values were normal at that time. Urinalysis on both occasions was negative, and the specific gravity was 1.015 and 1.020 on 2 specimens.

The blood pressure was 120/80. There were no positive physical findings except for mild joint enlargement of the fingers. A stool was negative for occult blood.

The patient was admitted to the Albany Hospital on November 10. Examination of the blood showed a hemoglobin of 9.8 gm. per 100 ml., a red-cell count of 3,010,000, a hematocrit of 29 per cent and a white-cell count of 7250 with a normal differential. The specific gravity of the urine was 1.003, and the examination was otherwise negative. A urinary Sulkowitch test was + + +. An intravenous phenolsulfonphthalein test showed an excretion of 16 per cent in 2 hours. The nonprotein nitrogen was 60 mg., and the creatinine 2.6 mg. per 100 ml.; the calcium was 7.2 milliequiv., and the inorganic phosphorus 2.1 milliequiv. per liter, and protein nitrogen was 64 mg., and the creatinine 3.0 mg. per 100 ml. She was last seen on June 22, 1954, when she felt quite well. The nonprotein nitrogen was 41 mg., and the hemoglobin 12.55 gm. per 100 ml.; the red-cell count was 4,250,000, and the hematocrit 41 per cent.

This patient had been treated by her family doctor for undiagnosed anemia. She was seen shortly after the diagnosis of vitamin D intoxication was made in Case 1. The diagnosis was quickly established, but recovery from the impairment of renal function was very slow. The blood values returned to normal in about seven months.

CASE 3. G. M., a 54-year-old woman, was admitted to the Albany Hospital on March 7, 1954, with major complaints of insomnia and extreme nervousness. These symptoms had been present for 3 months and were associated with vomiting and anorexia, a weight loss of 20.4 kg. (45 pounds) and marked mental depression. Before admission she had been studied at a hospital in an adjacent community largely because of a severe anemia. Examination of the blood in February, 1953, showed a hemoglobin of 8.3 gm. per 100 ml., a red-cell count of 3,300,000 and a nonprotein nitrogen of 103 mg. per 100 ml. The urine had a specific gravity of 1.004 and gave a + + test for albumin. The patient was given 4 transfusions before she was examined at the Albany Hospital.

Physical examination revealed an extremely depressed, agitated and confused woman. She was originally treated in

the psychiatric ward of the hospital because of frankly psychotic behavior. Mental symptoms required sedation and chlorpromazine to control her activities. The blood pressure was 110/80. No abnormal findings were present except for grayish pigmentation of the skin.

Initial laboratory studies showed nonprotein nitrogen to be 78 mg. and the creatinine 7.1 mg. per 100 ml. The specific gravity of the urine was 1.005. There was a trace of albumin, but no formed elements were seen on microscopical examination. The hemoglobin was 12.0 gm. per 100 ml., the red-cell count 4,180,000, and the hematocrit 40 per cent, and the white-cell count was normal (these figures were obtained after 4 blood transfusions).

The patient was seen by an endocrinologist, who thought that vitamin D intoxication, either superimposed on chronic renal disease or as a primary disease, was the most probable diagnosis. Intravenous fluid therapy was instituted at once, and later the patient was placed on a low-calcium diet. She showed marked improvement in her psychiatric state and general status on this regimen. On March 29, the nonprotein nitrogen was 62 mg., and the creatinine 2.9 mg. per 100 ml.

This patient presented a severe psychiatric problem, marked azotemia and severe anemia. Diligent "detective" work was necessary to establish the intake

TABLE 2. *Clinical Features.*

SUBJECT	MAJOR COMPLAINTS	WEAKNESS & LETHARGY	INSOMNIA	NOCTURIA	POLYURIA	GASTROINTESTINAL SYMPTOMS	BLOOD PRESSURE	PHYSICAL FINDINGS
Case 1	Fatigue; nausea; anemia; headache.	Marked	—	Moderate	Moderate	—	100/60	Gray skin
Case 2	Unexplained anemia; insomnia.	Mild	Marked	Moderate	Moderate	—	120/80	Osteoarthritis
Case 3	Anorexia; severe mental depression; unexplained anemia & azotemia.	Mild	Marked	—	—	Anorexia; nausea.	110/80	Gray skin
Case 4	Fatigue; unexplained anemia.	Marked	—	—	—	Nausea	140/80	None

The patient was seen in consultation by the hematologic service because of an unexplained anemia. On careful questioning she stated that she had been taking a "sunshine" vitamin for about 3 years. Her physician denied prescribing vitamin D, but a direct telephone call to her pharmacist, utilizing the prescription number, revealed that she had been taking "Darthronol," 1 capsule before each meal, since March 11, 1952, presumably for arthritis. The diagnosis of uremia due to vitamin D intoxication was strongly considered, and additional studies were ordered. The calcium was 5.7 milliequiv., and the inorganic phosphorus 2.3 milliequiv. per liter. Several stools were negative for occult blood. Sternal-marrow aspiration revealed moderate hypoplasia of the erythrocytic series but was otherwise negative. Phenolsulfonphthalein excretion was 4 per cent in 2 hours and 8 per cent at a repeat examination. A plain film of the abdomen showed no renal calcification. The bones appeared normal.

of vitamin D. The diagnosis in this case may well be chronic renal disease with superimposed vitamin D intoxication, but there can be no question that the vitamin intake was of considerable importance. Furthermore, marked symptomatic improvement followed proper diagnosis. Sufficient follow-up data on the anemia or renal disease are not available, but the patient is reported to have been clinically well for two years.

TABLE 3. *Laboratory Data and Drug Intake.*

SUBJECT	NONPROTEIN NITROGEN*	CREATININE†	CALCIUM‡	PHOSPHORUS§	ALKALINE PHOSPHATASE¶	URINARY FINDINGS			DRUG INTAKE
						SPECIFIC GRAVITY	ALBUMIN	PHENOLSULFONPHTHALEIN EXCRETION	
	mg./100 ml.	*mg./100 ml.*	*milliequiv./liter*	*milliequiv./liter*	*units*			*% in 2 hr.*	
Case 1	64.0	4.5	7.1	1.2	1.2	1.007	Negative	10	Darthronol, 150,000 to 300,000 units daily for 6 yr.
Case 2	60.0	2.6	7.2	2.1	0.6	1.003	Negative	16	Darthronol, 50,000 to 100,000 units daily for 3 yr.; weekly injections of vitamin D for about 10 yr. (amount unknown).
Case 3	103.0	7.1	5.7	2.3	0.6	1.004	Trace	8	Darthronol, 150,000 units daily for 2 yr.
Case 4	22.5‖	—	5.7	1.8	—	1.011	Negative	90	Vitamin D, 150,000 units daily for 3 yr.; drug stopped for 1-2 mo. on several occasions.

*Normal, 25 - 40 mg. per 100 ml.
†Normal, 0.8 - 2.0 mg. per 100 ml.
‡Normal, 4.8 - 5.5 milliequiv. per liter.
§Normal, 1.7 - 2.8 milliequiv. per liter.
¶Normal, 0.1 - 1.0 units.
‖Blood urea nitrogen — normal, 10-15 mg. per 100 ml.

CASE 4. G. T., a 50-year-old woman, was studied as an outpatient in February, 1955, because of an unexplained anemia. She had been in good health until June, 1954, when she had a gastrointestinal upset lasting 1 week. A

similar episode occurred in January, 1955; a blood count at that time was reported as low. (During World War II she had given frequent blood donations and had been told that her blood was normal.) She felt less energetic than usual for several months and noticed that her work capacity was diminished. There were no urinary symptoms. She was referred to a radiologist for study because of the anemia and unexplained gastrointestinal symptoms. Barium-enema study was negative, and an upper gastrointestinal and gall-bladder series and an x-ray film were normal. Sigmoidoscopy was negative. X-ray films showed a bone infarct in the neck of the left femur; a small area of calcification was present in the trochanteric bursa (these studies were repeated 9 months later and were unchanged).

Direct questioning elicited the fact that this patient had taken vitamin D capsules of 50,000 units, 3 daily, since December, 1951, for a painful arm after an injury. This was reduced to 2 capsules daily 1 year later. She stopped the drug for about 1 month on 2 occasions because of nausea and noticed some relief of symptoms. She had resumed the drug for 2 weeks before her visit. She had been treated with vitamin B_{12} and iron, without improvement.

Physical examination was negative. The blood pressure was 140/70. Examination of the blood revealed a hemoglobin of 10.75 gm. per 100 ml., a red-cell count of 4,010,000, a hematocrit of 32.5 per cent, and a white-cell count of 8500, with a normal differential; reticulocytes numbered 1.4 per cent. The plasma was not icteric. The urine was normal except for a specific gravity of 1.011 and a +++ Sulkowitch test. The nonprotein nitrogen was 36 mg. per 100 ml. (a determination of the blood urea nitrogen at another laboratory in January was reported as 22.5 mg. with a normal of 15 mg. per 100 ml.). Excretion of intravenously administered phenolsulfonphthalein was normal. The calcium was 5.7 milliequiv., and the inorganic phosphorus 1.8 milliequiv. per liter. A bone-marrow aspiration was entirely negative.

In view of the unexplained normochromic anemia and the history of vitamin D intake the diagnosis of hypervitaminosis was strongly suspected. The patient was advised to stop therapy and to avoid milk. She was told to increase her fluid intake by mouth. One month after she was first seen she noticed a striking change in her work tolerance and sense of well-being. On April 29 the hemoglobin was 12.0 gm. per 100 ml., and the hematocrit 37 per cent. On May 10, the corresponding values were 12.3 gm. per 100 ml. and 38 per cent. She was last seen on September 20, when she was quite well and had normal blood values.

This patient was studied as an outpatient because of fatigue and an unexplained anemia. The illness was the mildest in the 4 cases reported, and complete remission was achieved in a very short time.

Discussion

At present there seems little justification for the therapeutic use of vitamin D in a wide variety of conditions such as arthritis, allergic diseases such as asthma and pollinosis, psoriasis, acne, sarcoid and trichinosis. However, the cases reported above and in the literature concerning vitamin D intoxication, particularly in adults, have occurred either as toxic manifestations of the therapeutic use of the vitamin or because of injudicious self-medication. It is interesting that the multivitamin preparations "Darthronol" and "Dalsol" are available without prescription and contain 50,000 units of vitamin D per capsule. In addition most of the major drug companies have available therapeutic vitamin D preparations.

Vitamin D has been used for about twenty-five years in the therapy of the conditions mentioned above. In 1942 one of the earliest adult case reports on the toxicity of this drug appeared.[3] Nine years later 111 cases had been published, to which Chaplin et al.[2] added 12 in adults. The majority of these 123 patients were children. Twenty cases not included in the review of Chaplin, Clark and Ropes[2] were reported in 1948,[1,4] and scattered single cases have been recorded since then.[5-7]

The clinical features of the 4 patients described above are similar to those usually mentioned in vitamin D intoxication, but the manner in which they were encountered and the presenting problem of anemia have not been stressed in the literature. Certainly, vitamin D intoxication has not been mentioned under the differential diagnosis of anemias. These patients' symptoms consisted of fatigue, insomnia, weakness, anorexia, polyuria and nocturia, headache and in 1 case, marked psychiatric difficulties. The symptomatology of the syndrome is well described by Chaplin et al.,[2] who group symptoms under general — weakness and fatigue, with weight loss; gastrointestinal — nausea and vomiting, cramps and diarrhea; neurologic — headache, paresthesias and vertigo; psychiatric — depression; urologic — frequency and nocturia; and abnormal calcifications. None of these 4 patients showed abnormal calcification although this particular feature has been repeatedly described as one of the most striking clinical features.[5,8,9] Renal failure has been consistently emphasized, and all 4 of these patients had varying degrees of renal impairment, confirming the fact that the kidney is one of the most vulnerable organs to vitamin D poisoning. Certain features of the renal failure should be emphasized. In the first place none of these patients had hypertension. Secondly, the specific gravity was extremely low in all, the highest value being 1.011. Thirdly, albuminuria was minimal, and formed elements largely absent. Phenolsulfonphthalein excretion was markedly abnormal in 3 of the 4 patients. Azotemia was usually moderate but in Case 3 was extreme. The other laboratory findings that are part of this clinical entity are the derangements of calcium metabolism. Classically, a hypercalcemia, normal or slightly elevated phosphorus and normal or slightly elevated alkaline phosphatase are found. In these patients the calcium was greatly elevated in 2 cases and only slightly elevated in the others. The phosphorus (inorganic) was normal in 3 patients and moderately depressed in 1. The alkaline phosphatase was normal in all.

The mechanism of vitamin D intoxication is believed by Albright and Reifenstein[10] to be primarily an increase in the normal physiologic activity of vitamin D — namely, increased calcium absorption from the intestine. The other action of vitamin D, increasing phosphate excretion in the urine, is not believed to play a major part in the abnormal physiology associated with overdosage. The sequence of events proposed is that increased gastrointestinal absorption of calcium leads to an increased serum cal-

cium, which depresses parathyroid activity, and consequently decreases urinary phosphate excretion. As a result the blood is supersaturated with calcium and phosphorus, with resultant precipitation of calcium phosphate at abnormal sites. The 4 patients described above demonstrated only one finding suggesting hypercalcemia clinically, and that was a band keratitis in Case 1. All x-ray studies were nonrevealing, including plain films of the abdomen taken for gross renal calcification.

There are two schools of thought concerning the mechanism leading to renal disease. Albright believes that it is basically an abnormal deposition of calcium in the renal tissues, with subsequent interference with normal renal function. A second theory, proposed by Reed, Struck and Steck,[16] is that vitamin D is a tissue toxin in high doses and that local tissue damage occurs with secondary deposition of calcium.

The anemia in the cases presented above varied, with hemoglobin levels from 8.3 to 10.75 gm. per 100 ml. In the 3 patients who were seen before transfusions hematologic indexes were available. The anemia was uniformly normochromic and normocytic. Peripheral blood smears revealed nothing that contributed to the etiologic diagnosis or classification of the anemia. There was no reticulocytosis or hyperbilirubinemia to signify hemolytic disease. Bone-marrow study with the particle technic[11] revealed no diagnostic findings. The bone marrow in 2 cases was considered normal. One marrow (Case 1) showed an abnormal increase in hemosiderin and was hypercellular. The other (Case 3) exhibited a moderate erythrocytic hypoplasia. It is apparent that no specific etiology could be ascertained from all the available hematologic data.

Two possible explanations for the occurrence of anemia in these patients are suggested. Vitamin overdosage may have a direct effect on the bone marrow itself. Although this cannot be excluded it seems more likely that the anemia is due to the azotemia accompanying reduced renal function. All the patients described above had azotemia, the least renal impairment being evident in the one (Case 4) who presented the mildest anemia; furthermore, this patient recovered most rapidly, although the blood responded after the renal function became normal. The other patients exhibited a rough parallelism between the degree of renal improvement and the level of the blood values. The normocytic, normochromic type of anemia is most common in uremia, as pointed out by Callen and Limarzi[12] in their analysis of 102 patients. That group of patients revealed rare reticulocytosis although recent observers have pointed out that occasional cases of anemia due to uremia are hemolytic.[13,14] In their description of the bone marrow in uremia there was no diagnostic finding. However, a moderate general hyperplasia was common, and some granulocytic increase was present. When the nonprotein nitrogen reached very high levels erythrocytic hypoplasia occurred in some cases, and it is interesting that Case 3, who had the severest degree of anemia, demonstrated these changes in the bone marrow. The findings described by Callen and Limarzi are generally in agreement with our own studies on the bone marrow in uremic patients — it is essentially nondiagnostic.

A review of the cases of vitamin D intoxication reported in the literature reveals a striking consistency in that anemia is present in varying degrees in almost all patients who have renal involvement. The 7 patients of Chaplin et al.[7] had hemoglobin values ranging from 7.5 to 10 gm. per 100 ml. All but 1 had azotemia. No bone-marrow descriptions or hematologic indexes were given. Of the 111 cases tabulated in their review blood counts were listed in 12, with a range of hemoglobin from 8.0 to 12.0 gm. per 100 ml. Seven patients of the 11 described by Howard and Meyer[1] (10 were receiving vitamin D because of arthritis) had hemoglobin levels below 12 gm. per 100 ml.; the anemia was characterized as hypochromic, but calculations from the reported blood counts indicate that the anemia was normochromic in their patients. Schneider and Kammer[4] reported 9 cases. In the 7 in which blood counts were recorded the anemia varied (hemoglobin levels of 6 to 11.5 per 100 ml.). All these patients were azotemic. The other individual case reports already mentioned presented anemia of varying degree when blood counts were listed. No bone-marrow studies or hematologic indexes were described.

The amount of vitamin D and the time necessary for toxic effects to occur are extremely variable. The shortest period reported was twelve days at a dosage of 750,000 units daily.[8] Apparently, toxicity is largely a manifestation of individual susceptibility although it is also true that a high-calcium diet potentiates the toxic effects of the vitamin. In the 4 cases reported above, the exact dosage was difficult to determine with accuracy, but the patients had all ingested the drug for several years usually in the amount of 50,000 to 150,000 units daily.

The diagnosis of vitamin D intoxication depends on the physician's thinking of the disease and obtaining a history of vitamin D intake. The importance of this diagnosis is readily apparent since this is one of the reversible renal disorders. Furthermore, prognosis is quite variable, and kidney impairment may persist for years, emphasizing the fact that early diagnosis is essential. The clinical problem, consisting of anemia, azotemia and abnormalities of calcium metabolism, suggests several other diseases. Multiple myeloma, primary hyperparathyroidism, the syndrome of hypercalcemia and alkalosis described by Burnett et al.[17] and hyperparathyroidism secondary to chronic renal disease are most important in the differential diagnosis. The history, again, is of paramount importance. Bone-marrow and bone x-ray studies and protein abnormalities are most im-

portant in the diagnosis of myeloma. A low phosphorus and elevated alkaline phosphatase favor hyperparathyroidism, but, as in Case 1, repeated follow-up laboratory studies may be essential to establish the diagnosis. An elevated phosphorus and alkaline phosphatase suggest hyperparathyroidism secondary to renal disease.

Therapy of vitamin D poisoning is relatively simple. Withdrawal of the drug is mandatory, and a low-calcium diet and high-fluid intake are adjuvant measures. Transfusions have not been necessary in our patients. Stilbestrol has been suggested by Chaplin, Clark and Ropes[2] to increase the excretion of calcium as calcium citrate in the urine. Cobalt,[15] which has been used with some success in the treatment of anemia of uremia, might be considered. We did not choose to try this method of therapy. The chelating agents should be mentioned, but we have had no experience with them in this situation.

Summary and Conclusions

Four patients with the diagnostic problem of unexplained normocytic, normochromic anemias refractory to therapy are described. The diagnosis of vitamin D intoxication was established primarily by a history of vitamin D ingestion for long periods. Laboratory studies, particularly nonprotein nitrogen, calcium and phosphorus, and renal-function tests further clarified the clinical problem. It is concluded, from these cases and those reported in the literature, that anemia is present in almost every case of vitamin D intoxication and that these patients usually have varying degrees of azotemia.

The type of anemia, the hematologic findings and the bone-marrow studies are described. Although it is a matter of conjecture, we consider this anemia to be due to the azotemia present although a direct toxic effect on the bone marrow cannot be excluded.

The diagnosis of vitamin D intoxication depends largely upon suspecting the disorder in cases of azotemia and anemia of obscure origin. Prognosis is variable, and renal and hematologic abnormalities may persist for long periods despite striking symptomatic improvement.

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ACCIDENTAL INJURIES TO CHILDREN

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BOSTON

THE great advances in medical science have markedly changed the spectrum of conditions affecting the life and happiness of children. With the control of infantile diarrhea, diphtheria, tuberculosis, pneumonia and other conditions, the problem of accidental injury and death has come to the fore. Accidents are now the chief cause of death in children from one through sixteen years of age. In spite of the fact that this has frequently been called to their attention, physicians are still under the influence of the past and tend to dramatize epidemic disease and close their eyes to the greatest killer.

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In 1955 an epidemic of poliomyelitis swept over Massachusetts. In Greater New Bedford, comprising the city of New Bedford and the towns of Acushnet, Dartmouth and Fairhaven, with an estimated total population of 100,000, there were 57 reported cases, including 2 deaths, among children under seventeen years of age. During the same year 1861 accidental injuries were reported among children under seventeen in these four communities. Seven of these accidents resulted in death. Whereas the year 1955 was an epidemic year for poliomyelitis, available statistics show that in these four communities it was an endemic year for accidental injuries to children. It is entirely probable that other communities in New England mirror year after year the tragic experience of Greater New Bedford.

The tragedy lies not only in the loss of young lives and the crippling of others but also in the general

apathy of the public to the toll of accidents among children as contrasted to the great concern over the threat of statistically less important conditions, such as poliomyelitis. The possibility of the discovery of a preventive for poliomyelitis led parents to demand vaccine for their children. Yet, although the means of preventing the majority of the serious accidental injuries to children lie at hand, parents and communities appear to need stimulation and direction to initiate the simple common-sense steps to obtain these preventives. Many of these steps require less effort than taking a child for a poliomyelitis vaccination or for setting up a community inoculation program. Thus, the problem encompasses both the high incidence of accidents among children and the great need of community action to attack this major cause of morbidity and mortality among the young.

The Plan

In 1953 the Massachusetts Department of Public Health applied to the Charles H. Hood Dairy Foundation for a grant for a children's accident-prevention program. This application was approved, and the funds requested were made available for a three-year program. The original request was based on a statewide program. A State Advisory Committee on Children's Accident Programs was called together in Boston to outline a plan of action. This committee is composed of pediatricians, public-health workers, and other interested people and has met two to three times a year since the fall of 1953. The Committee decided with the approval of the Hood Foundation that a program would be of more value if based in one community rather than dispersed through the Commonwealth. Therefore, Greater New Bedford was chosen chiefly because of the interest of one of us (G. W. S.), who is a practicing pediatrician in that community. In initiating the program it was decided to gather reports on the accidents occurring to children and present them to a local committee consisting of leading citizens with the hope of involving them specifically with the problem in the community and thus stimulating them to take action to prevent such accidents.

It was believed that information on the local problem would be much more meaningful to the committee than statistics from the National Safety Council or information gathered from other programs.

The Operation

In December, 1953, the operation began. Sponsorship was obtained from the New Bedford Medical Society and St. Luke's Hospital in that city. A program director was appointed and opened her office in St. Luke's Hospital. We were fortunate in obtaining for director a person who had a wide knowledge of the community and a real interest in children.

Letters were sent to all physicians in the area over the signature of the president of the New Bedford Medical Society, enclosing forms for reporting accidents to children of sixteen years of age and younger. Reporting was also established through the Out-Patient Department and the Emergency Wards of St. Luke's Hospital and other hospitals in the area. Public-health nurses, the school department and the police department were also requested to report accidents occurring to children in this age group. As the accident reports began to come in, the director of the program made home visits in certain cases. In the first year these amounted to 22 per cent of all accidents reported. At the home visit she was able to obtain more complete information concerning the circumstances surrounding the accident. The information gathered through home visits has been difficult — in fact, impossible — to analyze statistically, but it has increased our knowledge of the facts surrounding accidents occurring to children. The local advisory committee was formed and has met monthly since February, 1954. This committee consists of local and state legislators, clergy, representatives of the health, school, fire and police departments, druggists, master barbers and other groups. The composition of this committee has changed from time to time. New members have been added when, because of their position or influence, they could further the program by initiating certain community action. The initial idea of having this group discuss accidents as reported and attempt to determine how they could be prevented by community action has not been followed out. Rather, the Committee has acted as a forum where the general problems of accident causation in the community have been discussed. At each meeting assignments were made to the individual members who were expected to report progress at the next meeting. These assignments included fact finding and the implementation of actions recommended by the Committee. Later, the Committee discussed the statistical analysis of the accidents occurring among children in New Bedford, and specific programs were based on the analysis of the statistics.

Excellent newspaper and radio coverage was given to the project. The community became very much interested in what was going on, and many service clubs and other groups demanded a part in the program and asked how they could help prevent accidents occurring to children in Greater New Bedford. So many requests came in that the staff was not able to handle them. It was decided that a person experienced in community organization was needed to implement the action of these different groups. Since funds were not available, a health educator was obtained on loan from the Massachusetts Department of Public Health for two days a week beginning in April, 1955. With the help of the educator, the community-organization program has gone ahead, and in January, 1956, the Hood Foundation made available additional funds and the health educator was

added to the staff on a full-time basis. During the entire period of operation the program has had the support and backing of the New Bedford Medical Society and the full co-operation of St. Luke's Hospital, which provided office space, heat and light and local telephone service free of charge.

TABLE 1. *Number and Percentage of 1861 Accidents, According to Severity (1955).*

SEVERITY	NUMBER	PERCENTAGE
Slight	1017	55
Moderate	731	39
Severe	99	5
Fatal	7	*
No report	7	*
Patients hospitalized	102	5

*<0.5%.

ACCIDENTAL INJURIES TO CHILDREN IN GREATER NEW BEDFORD

The statistics collected during 1954 and 1955 have given information about the problem of accidents occurring to children. Specific data regarding the frequency, types and causes of such accidents are vital for the development of a realistic attack on the problem as it exists.

A word of caution regarding the reliability of these statistics is indicated. We realize that the accident reports as submitted are incomplete and do not represent the total number of child accidents occurring in the community. However, we believe that they reflect with some degree of accuracy the major problem areas. This subject is discussed in greater detail below.

Tables 1-5, compiled from the accident reports for 1955, give some of our findings. The statistics for 1954 are almost identical.

Table 1 shows that 44 per cent of the accidental injuries reported were considered to be either moderately severe or severe. Five per cent of all the patients required hospitalization.

Table 2 shows that falls caused 39 per cent of the injuries, impact, such as that caused by a collision or blow, 29 per cent, cutting or piercing, 12 per cent, dog bite, 6 per cent, poison, 5 per cent, burns, 3 per cent, crushing, 3 per cent, and swallowing of a foreign body, 2 per cent.

Table 3 demonstrates the interesting fact that under one year of age there is no significant difference in the number of injuries occurring to boys and girls. However, in all other age groups many more accidental injuries occur to boys. In fact, over ten years of age, boys sustain twice as many accidental injuries as girls. It is of interest that by scene of accident more accidental injuries occur indoors to older girls than to older boys and that there is little sex difference in the age group regarding motor-vehicle accidents whereas there is considerable sex difference in pedestrian, bicycle, nontraffic and school accidents, in all of which injuries to boys predominate. The fact that almost twice as many of the total accidents occur to boys gives an impetus to concentrate a great deal of the preventive program on the male sex. This sex differential is, of course, directly linked to the difference in exposure to risk.

Table 4 summarizes the number of accidents according to source of reporting. The hospital emergency room sent in 66 per cent of the reports. It is interesting that of the 147 accidents reported by physicians, 83 were reported by the physician directly associated with the project. The number of reports from schools is very low. We have learned that approximately 200 accident reports from the schools have not as yet reached us. These accidents we believe to be mainly slight, since the more severe cases reached us through the reports of the hospital emergency room.

TABLE 2. *Number and Percentage of 1861 Accidents, According to Cause (1955).*

CAUSE	NUMBER		PERCENTAGE
Fall —	730		39
Fall, same level	325	18	
Fall, different level	359	19	
Fall, level not reported	46	2	
Impact	541		29
Cutting or piercing	209		12
Bite — total	118		6
Dog bite	111	6	
Other bites	7	*	
Poison (swallowed)	94		5
Burn	54		3
Crushing	50		3
Foreign body	43		2
Other causes	4		*
Cause not reported	18		1

*<0.5%.

Table 5 shows the number of accidents reported according to sex and age and demonstrates the rate per 100 population in the different age and sex groups. This illustrates again the greater vulnerability of boys than girls in all age groups over one year. This again illustrates the risk differential.

The following case reports are of severe and moderately severe accidents, as compiled by the Program Director after home visits:

Fall

CASE 1. L. B., a 5-month-old female infant, sustained a depressed fracture of the skull in the kitchen of her home. The mother, who was changing the baby's diaper and shirt, dropped the shirt and bent down to pick it up. She did not have a hold on the baby, who rolled off and struck her head on a corner of the radiator. The mother said that she usually strapped the infant on the bathinette. On this day she seemed to be in a greater hurry and to have more things to do than usual. On this day she was also taking care of

her 2 nephews (9 and 2 years of age) because her mother, who usually took care of them, had gone to a funeral.

Burn

CASE 2. R. B., a 21-month-old boy, received 1st-degree and 2d-degree burns of the chin, shoulder and chest in the pantry at home. The mother was preparing to cook French fried potatoes and put some shortening on a pan to melt. While waiting for the shortening to melt, she decided to take care of some diapers in the bathroom. She later looked into the pantry to see how things were ("had a feeling the baby might be up to something"). He was in the process of tipping over the pan on the stove. Some of the shortening spilled over — burning his chin, shoulder and chest.

Crushing

CASE 3. G. S., a 21-month-old girl, received a contusion of the left lower arm at home, in the kitchen, where the mother was washing clothes, using an old type of electric washer. When the mother went outdoors to hang out a piece of clothing she left the wringer in operation. The child followed the mother to the door. Outside, a neighbor called and the mother took a minute to chat. While talking, she heard the child cry out. Upon investigating, she found the child's arm caught in the wringer. The child had pulled a chair over to the washing machine and climbed up.

The mother stated that she was in a hurry that morning (and "didn't feel too good, either") because she had to get things done so that she could get ready to go to work.

Poison

CASE 4. M. R., a 3-year-old girl, swallowed 25 aspirin tablets at home in the bathroom. After being put to bed she got up and went to the bathroom (next to the bedroom). The mother heard water running. (On occasion the child got up for some water.) The mother went to the stairway and told the child to get to bed. About 5 minutes later she was up again to get some water. When the mother went to the stairway this time, she saw the child with a bottle in hand. Upon questioning, the child answered that she had been pretending to give her doll medicine. Since the doll could not swallow them, she took the pills. The bottle was about half full (it held 50 tablets). During the week before, the child had had a cold, and the mother had given her aspirins. The child knew where they were. She had to climb on the clothes hamper to reach the bottle, which had been placed on a high shelf.

Dog Bite

CASE 5. E. B., a 5-year-old girl, received lacerations of the right cheek, in 2 areas. She was in a neighbor's yard 2 houses away, where the children she played with lived. She was crouching on the ground drawing a picture with a piece of wood. A dog, owned by the man whose yard she was in, came close by and started to eat some garbage that had been left around. (The mother stated that the child had a phobia about germs and was very fussy about her eating habits.) She did not want the dog to eat the garbage, so she took a stick and began to shake it at the dog. Her face was near enough, where she was on the ground on her knees, so that as the dog went toward her it bit her face. This was a mongrel dog and not a very gentle dog. It was apt to turn on people; it chased cars that went by.

Cutting

CASE 6. S. R., a 7-year-old girl, sustained a laceration of the foot on a mechanical metal toy with sharp edges left on the living room floor. She had not put slippers on (was barefooted) and was hurrying around and did not see her toy. She stepped on it and cut herself.

Impact

CASE 7. T. P., an 11½-year-old boy, sustained a concussion in a fall from a bicycle. A group of youngsters were in the yard having a hot-dog roast. When it was almost time to break up and go home T. P. took the bicycle that belonged to one of the other boys, who started to run after him. T. P., showing off, told his friends to look — he could ride with no hands. The bicycle ran into a parked car, causing injury from impact.

PREVENTIVE MEDICINE

Interesting as statistics are, it is difficult to utilize them to measure the success or failure of the program. We have been warned against using activity counts in lieu of statistics.* We believe that a partially satisfactory method of measurement is the accomplishments of the Citizens Advisory Committee, which reflect the amount of community action taken as a result of the program. Certain definite accomplishments have taken place. In addition to these, a number of projects have been started that give excellent promise.

Some of the activities initiated by the Citizens Advisory Committee are outlined below. These projects were undertaken because a need for them was outlined either by the statistics collected or by a committee member or members.

Accidents at School

The Superintendent of Schools and the Agent of the Board of Health of New Bedford brought out early in the meetings that there was no clear plan for the referral of children injured in school. It appeared that only a physician could order an ambulance to take the child to the hospital. Frequently, a physician was not available, and there was a considerable time lag before the child got the care that he needed. The Committee was able to work out with the School Superintendent and the Agent of the Board of Health a plan whereby the person in authority at the school can order an ambulance to take the child to the hospital when necessary.

Burns

The Fire Chief, who is a member of the Committee, brought up the problem of the treatment of minor and major burns. He stated that the Fire Department was using information about the treatment of burns that had been obtained many years ago. The Committee asked the local medical society to consider this problem and received from it a report describing approved methods of treating minor and major burns. The Fire Chief has recommended that his staff follow these methods.

As a long-term result of this query by the Fire Chief, the American Academy of Pediatrics, through its surgical committee, is at present working to draw up recommendations for the treatment of burns. These recommendations will be published nationally.

*Report of working group on service programs. Basic principles governing statistics in public health. *Pub. Health Rep.* 71:521-524, 1956.

Safety Officer

It was brought to the attention of the Committee that there was no police officer in New Bedford whose specific duties were in the field of safety and accident prevention. Through the Committee, this fact was re-emphasized to the people of New Bedford Their activities have included the conduct of an area-wide poster contest to obtain an effective poster for warning parents of the dangers of accidental poisoning. Plans are being developed for an educational campaign in the fall to alert parents to the dangers of poisoning in children from common household substances.

TABLE 3. *Number of Accidents by Age and Sex According to Scene of Accident (1955).*

SCENE OF ACCIDENT	ACCIDENTS TO MALE PATIENTS											
	ALL AGES		UNDER 1 YR.		1-4 YR.		5-9 YR.		10-14 YR.		15-16 YR.		AGE NOT RECORDED	
Home accidents	628		15		305		193		87		24		4	
Indoor	268		12		192		40		13		9		2	
Outdoor	360		3		113		153		74		15		2	
Traffic accidents	281		2		81		98		74		25		1	
Passenger (motor vehicle)	94		2		41		20		16		15		—	
Pedestrian	87		—		27		48		11		—		1	
Rider of bicycle	100		—		13		30		47		10		—	
Nontraffic accidents	200		—		30		66		81		22		1	
School accidents	66		—		1		26		25		14		—	
Scene of accident not reported	34		—		6		13		14		1		—	
Totals	1209		17		423		396		281		86		6	

most concerned; as a result of their agitation, an officer has been appointed to the police force who at present devotes part of his time to the duties of a safety officer. It is hoped that in the near future he will be able to devote all his time to work in the safety field. A captain of the police force is a member of the Committee and was most helpful in pointing out this need to the Police Department.

Concerned with the high death rate among children from traffic accidents, the Committee has interested the community in obtaining a fellowship to permit a representative of the Police Department to attend a nine-month course in traffic-police administration at the Northwestern University Traffic Institute. This is a step toward a concerted attack on the traffic-accident problem. In addition the Police Department is pinpointing on a large-scale map of the city all child accidents reported as occurring outside the home in an effort to point out traffic and recreational danger spots.

Poisonings

On the recommendation of the Committee, the medical staff of St. Luke's Hospital has appointed a poison committee, which is drawing up information and policies and procedures concerning poisoning among children. A poison information center is being established at the Hospital. This will serve as a subcenter to the Boston Poison Information Center.

Local druggists, concerned with the high incidence of accidental child poisonings, have organized a committee to plan a community attack on the problem.

Fire Prevention

It was brought to the attention of the Committee by one of the members that a toy turning top, which is used by bakers to decorate birthday and party cakes, was highly flammable. The Committee purchased one of the tops and found this to be so. The Fire Chief has made a report, which has been circulated through the State Fire Marshal's Office to most of the communities of Massachusetts, describing this top and the dangers that might result from its sale. The people of Greater New Bedford and the bakers in this area have been alerted, and the top is being removed from sale and distribution. Other communities in Massachusetts have been warned through a news release to sixty-five newspapers.

Dog Bites

Accident reports have shown that there are a considerable number of dog bites occurring to children in the area. The Committee has encouraged the expansion of the demonstrations and talks that are made available to school children describing the care of animals.

School-Safety Education

Through the efforts of the Committee, an understanding has been achieved of the amount of safety education given in the New Bedford schools; the Committee has been working with the objective of increasing and strengthening this education, including the organization of school-safety patrols.

Playground Safety

Through the efforts of the Committee, a playground-safety project was started. This includes the teaching of first aid to playground supervisors (now a requirement for employment), the establishment of rules concerning giving of medical aid when a child is injured on the playground and the reporting and investigation of accidents so that environmental hazards may be eliminated.

Bicycle Safety

A bicycle-safety program has been developed, including classroom instruction on rules of the road and traffic regulations, mechanical inspection and Scotchliting of bicycles of children of the fourth, fifth and sixth grades and skill tests conducted as a bicycle rodeo to determine the youngsters' ability to ride safely.

Baby-Sitter Education

With the assistance of the staff, a five-hour course for teen-age baby sitters was organized under the sponsorship of the Young Women's Christian Association. This is the first of what is hoped will be a series of such courses. Prevention of common childhood accidents was stressed.

Parent Education

An experimental project in which all home accidents, their causes and methods of prevention are being recorded in log fashion for a period of three months by some 300 families is being attempted under leadership of parent-teachers associations to test the effectiveness of this device in reducing accidents in and around the home.

At the twice-weekly pediatric clinic, safety suggestions geared to specific hazards at specific age levels are being distributed to parents. Plans include the use of audiovisual materials such as pamphlet rack, exhibits and bulletin board.

A continuing channeling of child-safety information — based, of course, upon local accidents and problems — is carried on by means of feature and spot-news stories and photographs in the *New Bedford Standard-Times,* radio spot announcements and features, discussions among parent groups, service-club programs, displays and exhibits and so forth.

TABLE 3 *(Concluded).*

SCENE OF ACCIDENT	ACCIDENTS TO FEMALE PATIENTS											
	ALL AGES		UNDER 1 YR.		1-4 YR.		5-9 YR.		10-14 YR.		15-16 YR.		AGE NOT RECORDED
Home accidents	375		17		198		102		42		12		4
Indoor	217		16		137		34		18		8		4
Outdoor	158		1		61		68		24		4		—
Traffic accidents	156		2		43		65		30		14		2
Passenger (motor vehicle)	93		2		27		28		21		13		2
Pedestrian	43		—		14		26		3		—		—
Rider of bicycle	20		—		2		11		6		1		—
Nontraffic accidents	71		—		11		25		27		8		—
School accidents	28		—		1		17		5		5		—
Scene of accident not reported	19		—		3		10		4		2		—
Totals	649		19		256		219		108		41		6

Nursing Education

An in-service training program is scheduled in the fall for public-health nurses of the Greater New Bedford area. It will be aimed at promoting greater understanding of the human and environmental factors in the cause and prevention of accidents, and developing skills in translating safety knowledge into effective safety education during routine home visits and clinic conferences.

The Curriculum Committee of St. Luke's Hospital Nursing School is considering areas of the student-nurse teaching program in which increased emphasis on the importance of the child-accident problem will be introduced. Areas under discussion include home nursing, obstetrics, pediatrics, orthopedics, medicine, surgery and first aid.

All patients on the Maternity Service at the Hospital receive information and material on how to keep their infants safe.

Physician Education

Through the Medical Advisory Committee, attempts are being made to make physicians more aware of the magnitude of the accident problem among children in the community and to point out their role in alerting parents to common accident hazards that can be anticipated and prevented with parent co-operation. In addition the program is providing safety literature and home-safety check lists to physicians for distribution to parents.

Moreover, the New Bedford Medical Society has prepared a resolution to submit to the Massachusetts Medical Society stating that an accident-prevention committee should be set up in the Society. This committee would be concerned with accident prevention in all age groups and would consist of physicians working in pediatrics, adult medicine, industrial medicine and public health.

TABLE 4. *Number of Accident Reports and Percentage Distribution, According to Source of Reporting (1955).*

SOURCE OF REPORT	TOTAL REPORTS RECEIVED	
	NUMBER	PERCENTAGE
Hospital Emergency Room	1359	66
Hospital — other	122	6
Police	308	15
Physician	147	7
School	46	2
Nurse (board of health, visiting nurse)	37	2
Newspaper	33	2
Totals	2052*	100

*Greater than number of cases (1861); some accidents reported by more than 1 source.

Water Safety

Because accidental drowning is the second leading cause of accidental death to children in the New Bedford area, the Committee is seeking to focus attention of parents on the need and desirability of having children develop swimming skills and ability to handle small craft safely. It is also assisting local groups (particularly municipal-beach authorities) to expand swimming-instruction opportunities and supervised swimming-instruction facilities.

During the recent summer the number of children who learned to swim under municipal-beach supervision was doubled over that of last year, and funds for hiring additional water-safety instructors will be requested by the Park Department to permit expansion of the instruction program next year. Other activities this summer resulted in voluntary reporting of all accidents occurring to children at the public municipal beach; provision of first-aid equipment and supplies through the American Red Cross local chapter to the first-aid station of the children's beach; and the expansion of the Park Department's annual water carnival and swimming meet to include demonstrations of lifesaving technics for the swimmer and nonswimmer in small-craft accidents.

Evaluation of Results

It had been thought that the effectiveness of an accident-prevention program would be relatively simple to measure. It was planned that statistics indicating the frequency of accidents before the program was under way could be compared with similar statistics collected after the program had been in operation for a reasonable period. A successful program would show that there had been a decrease in the morbidity and mortality due to accidents between the two periods. However, we have found the evaluation not as simple as this. In the first place, it has been extremely difficult to find a stable basis of reporting. Reporting of accidents by physicians in Greater New Bedford has been very incomplete, the most complete reporting being obtained from the pediatrician who is directly connected with the project. However, even he found on certain occasions that he had failed to report accidents occurring to children whom he had treated. The reporting of accidents from the hospital emergency room seems to be on a more stable basis. However, on closer examination it becomes evident that the number of accidents referred to the emergency room is changing with changing patterns of medical practice in the community. With an increasing number of patients being covered by Blue Shield, many doctors are referring their accident cases to hospital emergency rooms, where they can do minor

TABLE 5. *Population under Seventeen Years of Age and Accidents Reported According to Age and Sex (1955).*

AGE	NEW BEDFORD METROPOLITAN AREA POPULATION (1950 CENSUS)			NO. OF ACCIDENTS REPORTED			RATE PER 100 POPULATION		
	TOTAL	MALES	FEMALES	TOTAL	MALES	FEMALES	TOTAL	MALES	FEMALES
yr.									
Under 1	2,269	1,116	1,153	36	17	19	1.6	1.5	1.6
1- 4	10,273	5,225	5,048	680†	423	256	6.6	8.1	5.1
5- 9	10,261	5,105	5,156	616†	396	219	6.0	7.8	4.2
10-14	8,405	4,202	4,203	389	281	108	4.6	6.7	2.6
15 & 16*	3,372	1,677	1,695	127	86	41	3.8	5.1	2.4
Not reported				13†	6	6			
Totals	34,580	17,325	17,255	1861†	1209	649			
Averages							5.4	7.0	3.8

*Population at age 16 not available; estimate made.

†Greater than sum of subdivisions; total includes accidents with sex not reported.

surgery with greater facility than in their private offices. On the other hand there has been an increase in the number of x-ray machines owned and operated by private physicians in New Bedford. This means that many patients with fracture and suspected fracture who were formerly given x-ray examination at the hospital are now being given such studies and treated in the doctors' private offices. Also, since the project was started, a change in hospital admitting policies has resulted in the admission of certain accident cases directly to an accident ward rather than through the regular admitting office. Thus, it is difficult in a city like Greater New Bedford to establish a firm baseline against which the success of an accident-prevention program may be measured.

A more definite measurement of success or failure would require a resurvey of the community three to five years after the program ends to determine which projects will have continued on as part of the community life and which will have been abandoned when the stimulus of the full-time staff will have been withdrawn. Such a resurvey would be of great value in delineating successful kinds of continuing programs in child-accident prevention. Here, again, caution must be voiced, however. We shall not be able to state that children's lives have been saved merely because the community continues any one or all of the programs.

Discussion

Accidents are now the major cause of death and a major cause of disability among children one through sixteen years of age in this country. The people of Massachusetts, who last year lived through a severe epidemic of poliomyelitis, may find this difficult to accept. However, poliomyelitis at its worst does not bring the harm to the young that accidents cause year after year.

We have described how the people of Greater New Bedford, Massachusetts, were stimulated to action against accidents. As a result of our experience, we believe that the success of the program depended on the following factors:

The collection and use of local statistics. This brings the community face to face with its own problem.

The utilization of a local advisory committee of members chosen not for their prominence but for their ability to get things done.

Medical leadership — the program in New Bedford would not have come about except for the medical leadership we had and the sponsorship of the Medical Society and St. Luke's Hospital.

Identification with the community. This program was financed by a private foundation through the Massachusetts Department of Public Health. However, great care was taken to ensure that this was a local project. All authority was vested in the local staff and advisory committee.

Summary and Conclusions

A children's accident-prevention program is described. Certain factors that appear to have contributed to the evidence of at least partial success of the program are noted. Other communities planning to attack this problem may find the discussion of value. It must be emphasized, however, that there is no clear blueprint for each community to follow. The best pattern is the one that utilizes the strength of the individual community.

We are indebted to the following members of the project staff: Miss Alice Miller, R. N., program director, and Miss Cecilia DiGicco, M. P. H., health educator, and to Miss Etta Bloom, statistician of the Division of Maternal and Child Health Services of the Massachusetts Department of Public Health, for their assistance in the preparation of this article.

PERNICIOUS ANEMIA IN CHILDHOOD*

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THE clinical and hematologic manifestations of pernicious anemia are due to a deficiency of vitamin B_{12} resulting from a specific and selective inability to absorb the vitamin from the gastrointestinal tract. The failure of absorption of vitamin B_{12} in pernicious anemia is due to the absence of intrinsic factor from the gastric secretion that is associated with, and generally considered to result from, atrophy of the gastric mucosa.[1] Achylia gastrica accompanies the atrophy of the gastric mucosa, and free hydrochloric acid is rarely present in the gastric secretion.

Vitamin B_{12} deficiency can be proved by serum microbiologic assay, but a deficiency of vitamin B_{12} is found in conditions other than pernicious anemia.[2] The diagnosis of pernicious anemia can be established, even in remission, by technics utilizing radioactive vitamin B_{12} since a diminished absorption of the vitamin that can be corrected by the administration of intrinsic factor is characteristic.[3]

Pernicious anemia is predominantly a disease of

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Supported in part by grants from the United States Public Health Service, the Squibb Institute for Medical Research and the Kentucky Research Commission.

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adult life and is rarely reported in persons under the age of thirty.[4] The disease has been described in children, but the diagnosis has not been unequivocally established in the majority of the reported cases.[5,6]

We have studied a seven-and-a-half-year-old Negro with a recurrent macrocytic anemia, megaloblastic transformation of the bone marrow, free hydrochloric acid in the gastric juice and vitamin B_{12} deficiency. A description of this case and studies that demonstrate the absence of intrinsic-factor activity in the patient's gastric secretion constitute the present report.

four hours by this method. The amount of radioactive vitamin B_{12} administered was 0.5 microcurie, with a specific activity of 760 microcuries per milligram of vitamin B_{12} and a concentration of 0.7 microgm. of vitamin B_{12} per 0.5 microcurie. The intrinsic-factor preparation used in these studies was a 30-mg. vitamin B_{12} free concentrate.

Gastric intubations were done with fluoroscopic control, and gastric juice obtained by continuous aspiration.

Gastric acidity was determined by pH meter, and

TABLE 1. *Hematologic Data.*

HOSPITALIZATION	DATES	HEMATOCRIT	HEMOGLOBIN	RED-CELL COUNT	RETICULOCYTE COUNT‡	WHITE-CELL COUNT	PERIPHERAL RED-CELL MORPHOLOGY	BONE MARROW	TREATMENT OF ANEMIA	REMARKS
		%	*gm./100 ml.*	*X10⁶*	%	*X10³*				
2	8-23-50*	12	3.1	1.25	1.6	4.0	Anisocytosis & poikilocytosis	Normoblastic	Whole blood & ferrous sulfate	At age of 2 yr. & 4 mo. good response; diagnosis, nutritional anemia.
	10-21-50†		12.4	4.2	0.6 (11.6)			Repeat megaloblastic	Rubrafolin§ & folic acid	
3	5- 5-52*	16	4.5	2.0	2.0	5.7	Normal	Erythroid hyperplasia	Folic acid (parenteral & oral) ferrous sulfate	At age of 4 yr. & 1 mo. free acid in gastric juice; diagnosis, "nonpernicious" macrocytic anemia.
	6-28-52†		10.3	4.81	0.2 (27.6)					
4	6-17-53*		3.7	1.42	0.4	2.9	Macrocytosis, anisocytosis & poikilocytosis	Megaloblastic erythropoiesis	(6-20-53) 30 microgm. of vitamin B_{12} intramuscularly	At age of 5 yr. & 2 mo. serum assay of vitamin B_{12} 0; 3 days after treatment, level 100 microgm./ml.; diagnosis, "nonpernicious" macrocytic anemia.
	7- 7-53†		9.2	3.89	0.8				After discharge 30 microgm. of vitamin B_{12} intramuscularly every 2 wk.	
5	2-24-54*		10.6			11.6				At age of 5 yr. & 10 mo. diagnosis cervical lymphadenitis
	2-27-54†									
6	5-27-54*		9.2	4.02		5.3	Normal		None	At age of 6 yr. & 2 mo. diagnosis left-lower-lobe pneumonia & "nonpernicious" macrocytic anemia
	6- 2-54†									
7	11-15-55	13.5	3.9	1.4	1.2		Macrocytosis	Megaloblastic	Bicillin (parenteral) & vitamin B_{12}	At age of 7 yr. & 7 mo. free acid & pepsin in gastric juice; vitamin B_{12} uptake test of Schilling positive; diagnosis, pernicious anemia.
	12-13-55	43.5	13.1		1.2 (48.4)					

*Admission.
†Discharge.
‡Greatest reticulocyte response given in parentheses.
§Available from E. R. Squibb and Sons, New York City.

MATERIAL AND METHODS

The serum vitamin B_{12} assays were performed by the method of Ross using *Euglena gracilis* as a test organism.[7]

Absorption studies with radioactive vitamin B_{12} containing Co^{60} were performed by the Schilling technic as modified by Tabern.[8] With this method 1 liter of unconcentrated urine is counted directly on a well scintillation counter, and the amount of radioactive material excreted is determined from a graph. Patients with pernicious anemia excrete less than 5 per cent of the administered radioactive dose in twenty-

pepsin determinations by the Mett method as modified by Nirenstein and Schiff.[9]

CASE REPORT

J.J., a 7½-year-old Negro, was readmitted to the Louisville General Hospital for the 7th time on November 15, 1955. He had been born in this hospital on April 1, 1948, weighing 3.3 kg. (7 pounds, 4 ounces), after an uneventful pregnancy and delivery. He was discharged as a normal newborn infant on the 4th hospital day and was seen on 2 occasions in well-baby clinics. At the age of 2 years and 4 months he was admitted to the Pediatric Service of the Louisville General Hospital with complaints of vomiting, loss of weight, paleness, fever and swelling of the eyes. Stool

examinations and x-ray studies of the skeleton, gastrointestinal tract and chest were negative. A standard glucose tolerance test and the total serum protein were normal. The clinical findings were interpreted as compatible with an iron-deficiency anemia (Table 1), and whole-blood transfusions, oral doses of iron and a hematinic agent containing folic acid and vitamin B_{12} were given. The response to therapy (Table 1) was considered adequate, and the patient was discharged after 2 months in the hospital.

He did not return for follow-up care and was readmitted at the age of 4 years and again at the age of 5 years and 2 months with severe anemia. The anemia on both occasions was attributed to a nutritional deficiency. The serum vitamin B_{12} level was 0 on the latter admission, and the anemia responded to vitamin B_{12} by injection (Table 1). After the fourth admission he received vitamin B_{12} by injection every 2 weeks until the 5th admission for an unrelated illness at the age of 5 years and 10 months. The hemoglobin at that time was 10.6 gm. per 100 ml. He was readmitted to the hospital at 6 years and 2 months of age for a left-lower-lobe pneumonia, which responded to antibiotics. The hemoglobin was 9.2 gm. per 100 ml., but he had not received vitamin B_{12} injections for 6 months. After this admission he was not seen again until 18 months later, when he complained of lethargy, pallor, weakness and swelling about the eyes.

Physical examination revealed a pale, fairly well developed, poorly nourished and chronically ill boy who was 24 cm. tall and weighed 15.2 kg. (33½ pounds). Puffiness was noted about the eyes, and the mucous membranes were pale. There was a generalized lymphadenopathy. The tongue was smooth and glistening, and the papillae were atrophic. The liver edge was felt 2 cm. below the right costal margin, but the spleen was not palpable. A complete neurologic examination revealed no abnormalities.

The temperature was 102°F., the pulse 130, and the respirations 36. The blood pressure was 100/70.

Hematologic values on this admission are shown in Table 1. Morphologically, the red cells were macrocytic. A bone-marrow specimen aspirated from a spinous process showed a maturation arrest of erythropoiesis at the megaloblast level. Three stool examinations were negative for occult blood, ova and parasites. A teleroentgenogram revealed a moderately enlarged, globular heart. No vitamin B_{12} was demonstrated in the serum by microbiologic assay. Studies with radioactive vitamin B_{12} disclosed poor absorption of the vitamin, and the administration of intrinsic factor corrected this absorptive defect. The patient's gastric juice did not enhance the absorption of radioactive vitamin B_{12} in a patient with proved pernicious anemia (Table 2). Gastric intubation under fluoroscopic control revealed normal gastric acidity (pH 2.10) and pepsin content. A vitamin A tolerance test with an oily preparation (Oleum Percomorphum) and a glucose tolerance test were negative. The patient was given benzathine penicillin G, 600,000 units intramuscularly a day, for reasons described below, but this failed to produce a significant reticulocyte response. On the 7th hospital day and daily thereafter he was given 30 microgm. of vitamin B_{12} intramuscularly, and a prompt reticulocyte response occurred, with subsequent correction of the anemia. He is now well and is receiving 30 microgm. of vitamin B_{12} intramuscularly every 2 weeks.

TABLE 2. *Absorption Studies with Radioactive Vitamin B_{12}.*

PATIENT	PROCEDURE*	EXCRETION
		%
J.J.	Vitamin B_{12} & CO^{60}	4.6
	Plus intrinsic factor	22.5
J.G.†	Vitamin B_{12} & CO^{60}	2.4
	Plus 85 ml. of gastric juice from J.J.	1.4
	Plus 85 ml. of gastric juice from normal control	44.0

*0.5 microgm. of vitamin B_{12} & CO^{60} orally.
†Proved case of pernicious anemia.

DISCUSSION

The first episode of this recurrent anemia, which occurred when the patient was two years old, was at first attributed to iron deficiency, but the hematologic data were not entirely consistent with this diagnosis. It seems likely in retrospect that the anemia was the result initially of vitamin B_{12} deficiency, and the subsequent course of the anemia is consistent with this interpretation. Vitamin B_{12} deficiency was first demonstrated by microbiological assay of the patient's serum during a relapse of the anemia that occurred when he was five years old, and this deficiency was attributed to dietary inadequacy.

A deficiency of vitamin B_{12} may be produced by a variety of mechanisms, such as dietary lack, competitive utilization of the vitamin by intestinal microorganisms or failure of absorption due either to a lack of intrinsic factor or to nonspecific alteration in the absorptive property of the intestine.[10] Dietary deficiency of vitamin B_{12} has been described in a rare group of vegetarians who exclude all animal protein from their diet. The deficiency of vitamin B_{12} occurs irregularly in such cases after several years of dietary restriction, and anemia is not a significant feature.[11] In fish-tapeworm infestation the parasite utilizes vitamin B_{12} in the intestine so that it is unavailable to the host, and the deficiency can be corrected by elimination of the parasite. A similar mechanism may be present in the patient with intestinal strictures or anastomoses that produce an alteration in the intestinal bacterial flora. The pathogenesis of the deficiency in patients with anatomic lesions of the small intestine has recently been discussed by Thompson and Ungley.[12] In sprue diminished absorption of vitamin B_{12} is the result of a diffuse, nonspecific alteration in the absorptive property of the small intestine and cannot be corrected by the administration of intrinsic factor.

The presence of vitamin B_{12} deficiency in the case reported above could not be attributed to any of the aforementioned factors. The nutritional history indicated an ample dietary intake of vitamin B_{12}. Radiologic examination of the gastrointestinal tract revealed no abnormalities, parasites were not found on repeated stool examinations, and vitamin A and glucose tolerance tests were not characteristic of the intestinal-malabsorption syndrome. The diagnosis of pernicious anemia was established by the patient's inability to absorb vitamin B_{12} and the absence of intrinsic-factor activity from his gastric juice.

The results of the studies with radioactive vitamin B_{12} are shown in Table 2. The absorption of the vitamin was greatly diminished in the patient, and the administration of intrinsic factor corrected the absorptive defect. Absence of intrinsic-factor activity was further demonstrated by the inability of the pa-

tient's gastric juice to enhance the absorption of vitamin B_{12} in another patient — an adult male with proved pernicious anemia in remission. The patient's freshly aspirated gastric juice did not enhance the absorption of vitamin B_{12} in the test subject whereas gastric juice from a normal boy produced normal absorption of vitamin B_{12} in the same subject.

In addition to the present report there are 5 examples of pernicious anemia in childhood in which the diagnosis has been proved beyond reasonable doubt[5,6,13,14] (Cases VZ and CZ of Reisner and his associates). Reisner et al.[6] reviewed the literature and accepted 12 cases as representing pernicious anemia in children, to which they added 4 of their own. Their criteria for acceptance of the previously reported cases were a macrocytic anemia with a megaloblastic bone marrow, exclusion of other causes of megaloblastic hematopoiesis and a necessity for continued therapy to prevent relapse. The diagnosis was not proved unequivocally in the majority of the cases fulfilling these criteria since other causes of vitamin B_{12} deficiency were not excluded and absence of intrinsic factor was not demonstrated.

On the basis of the findings in his patient Benjamin[13] suggested that pernicious anemia in childhood might represent a congenital deficiency of intrinsic factor. The delay in the onset of the disease was assumed to be due to the presence of normal stores of erythrocyte-maturing factor (vitamin B_{12}) at birth. Despite the failure of the infant to absorb vitamin B_{12} the manifestations of a deficiency would not be apparent until these stores were exhausted. Normal levels have been demonstrated in the cord blood of infants born of normal mothers,[15] and Mollin and Ross[16] have also reported normal levels in the serum and tissues of infants. A placental barrier to vitamin B_{12} cannot be demonstrated. The administration of 500 or 1000 microgm. of the vitamin intramuscularly to women in labor results in an increase in the vitamin B_{12} level in cord blood comparable to the increase in maternal blood.[15] The appearance of anemia during infancy is compatible with a congenital absence of intrinsic factor. Anemia has been present during the first two years of life in 3 of the proved cases of pernicious anemia in children; the earliest age at recognition was thirteen months.[5] The 3 other children with proved pernicious anemia were age thirteen, nine and eight and a half years when the diagnosis was established. Since it would be necessary to demonstrate diminished absorption of vitamin B_{12} at birth due to absence of intrinsic factor, proof of this concept is not available.

Achlorhydria is considered indispensable to the diagnosis of pernicious anemia, but free hydrochloric acid has been demonstrated in the gastric juice of 5 of the 6 proved examples of pernicious anemia in childhood. In 1 patient a gastric biopsy revealed a histologically normal gastric mucosa.[5] It is generally believed that the degenerative change in the gastric mucosa found in pernicious anemia precedes and results in failure to secrete intrinsic factor. According to Magnus and Ungley[17] the gastric lesion of pernicious anemia is histologically characteristic. Exfoliated cellular material from the stomach of patients with pernicious anemia reveals enlarged cells, which are apparently specific.[18] It has been suggested that the gastric lesion of pernicious anemia may be due to vitamin B_{12} deficiency.[5] The absence of atrophy of the gastric mucosa, as proved by biopsy in 1 case, and the presence of hydrochloric acid in the gastric juice of 5 of the 6 children with proved pernicious anemia support this hypothesis. In 3 of these children free hydrochloric acid was absent initially but was demonstrable after treatment. The findings in these children suggest that all the manifestations of pernicious anemia, including the atrophy of the gastric mucosa, are the result of vitamin B_{12} deficiency. The failure of treatment to correct the gastric lesion, which is generally observed, may be the result of prolonged deficiency producing an irreversible change. If this concept is correct, absence of intrinsic factor should be demonstrable in the patient with pernicious anemia before atrophy of the gastric mucosa, with achlorhydria, develops. Absorption studies with radioactive vitamin B_{12} make it possible to detect diminished secretion of intrinsic factor. Absorption studies in persons with a family history of pernicious anemia might aid in determining whether absence of intrinsic-factor activity precedes the development of atrophy of the gastric mucosa and achlorhydria.

Neurologic symptoms have been present in 2 children with pernicious anemia, but irreversible changes in the nervous system have not been described. No neurologic findings were present in the case reported above, despite the numerous relapses and prolonged vitamin B_{12} deficiency.

The megaloblastic anemias, in general, represent the hematologic manifestation of a deficiency of vitamin B_{12}, folic acid or, rarely, vitamin C. The mechanisms that produce vitamin B_{12} deficiency and their differentiation from pernicious anemia have been described.

Foy, Kondi and Manson-Bahr[19] have reported a megaloblastic anemia in South Africans associated with vitamin B_{12} deficiency that responded to oral or parenteral administration of penicillin. The beneficial action of penicillin is assumed to be due to the elimination of intestinal micro-organisms that competitively utilize vitamin B_{12}. The patient described above received benzathine penicillin, 600,000 units intramuscularly, every day for a week, but no significant hematologic response was noted.

Zuelzer and Rutzky[20] have described in detail the megaloblastic anemia of infancy, which is not recurrent and responds specifically to folic acid but not to vitamin B_{12}. This anemia is most frequent in the age range of eight to fourteen months, and the upper age

limit is eighteen months. The differentiation of this anemia from pernicious anemia in children on the basis of clinical and hematologic findings alone is difficult. The fact that the megaloblastic anemia due to folic acid deficiency is limited to the first eighteen months of life and does not respond to vitamin B_{12} is of value in differential diagnosis. Folic acid will produce a hematologic remission in both the megaloblastic anemia of infancy and pernicious anemia. The use of a multiple hematinic agent containing folic acid initially in the patient described above served only to obscure the diagnosis.

The familial occurrence of pernicious anemia is well known and a family history of pernicious anemia has been present in 3 of the children with proved pernicious anemia. It was not possible to obtain a complete family history from our patient, and only his mother and his brother were available for study. There was no evidence of vitamin B_{12} deficiency, as determined by serum microbiologic assay, in his mother or brother, but absorption studies with radioactive vitamin B_{12} were not performed. Consanguinity was present in the family of 1 of the children with

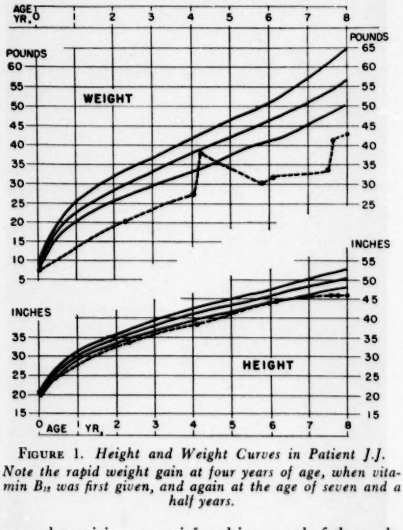

FIGURE 1. *Height and Weight Curves in Patient J.J. Note the rapid weight gain at four years of age, when vitamin B_{12} was first given, and again at the age of seven and a half years.*

proved pernicious anemia[5] and in several of the probable examples reported by Reisner et al.[6] There was no evidence of consanguinity in our patient's family as far as could be determined.

The recurrent vitamin B_{12} deficiency had no striking effect on our patient's growth and development (Fig. 1). His height was within the lower percentile for his age at the time of these studies. He gained weight rapidly after the administration of vitamin B_{12} on this admission, an observation that has been noted previously.[3] Further studies are in progress to evaluate the patient's growth and development while he is receiving vitamin B_{12}.

Pernicious anemia is uncommon but not extremely rare in Negroes. Seventeen per cent of the patients with pernicious anemia attending the Hematology Clinic of the Louisville General Hospital are Negroes. Our patient is the only Negro child with pernicious anemia described in the literature.

SUMMARY

Studies with radioactive vitamin B_{12} proved the diagnosis of pernicious anemia in a seven-and-a-half-year-old Negro boy with a recurrent megaloblastic anemia. Free hydrochloric acid was present in the gastric juice of the patient. The findings in the previously reported proved examples of pernicious anemia in childhood are discussed. It is suggested that the gastric lesion of pernicious anemia is a result of vitamin B_{12} deficiency and not a factor in the pathogenesis of the disease.

We are indebted to Dr. William Darby, of Vanderbilt University, for the vitamin A determinations and to Mrs. Eleanore K. LaBaw for the vitamin B_{12} and Mrs. Dorothy Anderson for the gastric pepsin and pH assays.

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CONGENITAL ESOPHAGEAL STENOSIS*

Report of a Case of Annular Muscle Hypertrophy at the Esophagogastric Junction

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CONGENITAL esophageal stenosis at the level of the cardia is an uncommon and poorly understood anomaly. Since the majority of these cases in infants respond satisfactorily to instrumental dilatation, the precise nature of the stricture is rarely determined. For this reason, an unusual case in which the obstruction was caused by an annular band of hypertrophic muscle is reported.

CASE REPORT

J. R. (B.H. 190203), a seven-week-old female infant, was admitted to the Babies Hospital of the Columbia–Presbyterian Medical Center on July 6, 1954, because of vomiting since birth. Soon after delivery it was noted that she accumulated excessive amounts of thick, colorless mucus in her oropharynx. Part or all of each feeding was regurgitated. Paroxysms of coughing and cyanosis frequently occurred when she nursed but were promptly relieved when she was turned upside down. A chronic cough and a hoarse cry had been present since the 2d day of life. Ten days before admission to Babies Hospital a severe episode of coughing and cyanosis led to her admission to another institution, where an emergency tracheostomy was performed.

The family history was noncontributory. She had been born at full term after a spontaneous breech delivery and had weighed 2827 gm. at birth.

Physical examination revealed a pale, undernourished infant, weighing 2980 gm., who was moderately dyspneic. The temperature was normal, and the pulse was 120 per minute. A fine papular rash was noted over the right side of the face, and there were many ecchymotic spots over both buttocks where intramuscular injections of procaine penicillin had been administered. A tracheostomy tube was present in the mid-line of the neck just above the suprasternal notch and was functioning satisfactorily. Direct laryngoscopy revealed a normal larynx. Breath sounds were diminished at the right base, and coarse rhonchi were audible over both lung fields. No other significant physical abnormalities were noted.

Routine laboratory studies were within normal limits, and a stool was guaiac negative.

Roentgenographic examination of the lungs revealed a small area of bronchopneumonia in the right lower lobe. An esophagogram with iodized oil (Fig. 1) showed an area of stenosis approximately 3 cm. above the level of the diaphragm that did not relax throughout the period of examination.

Under general anesthesia a 5-mm. esophagoscope could be passed 14 cm. from the level of the upper-gum margin. At this point the esophageal lumen coned down to an area of tight stenosis through which a filiform leader could not be passed. The mucosa of the esophagus appeared normal throughout.

One week after admission an exploratory left-sided thoracotomy was performed through the bed of the 8th rib. The lower esophagus was mobilized in the posterior mediastinum, and approximately 6 cm. of stomach was found herniated into the chest. The cardia was located 3 cm. above the lax diaphragmatic hiatus. A firm, "doughnut-like" ring of tissue, not unlike the tumor of congenital hypertrophic pyloric stenosis in consistence, could be felt at the esophagogastric junction. It was impossible to direct an indwelling No. 10 Fr. plastic nasogastric tube past this point by external manipulation. Accordingly, an extramucosal esophagocardiomyotomy was performed in the long axis of the esophagus through the thickened band, extending 1.5 cm. proximal and distal to it. The cut edge of the thickened band (Fig. 2) appeared roughly oval and pale gray, and the greater part of it projected toward the esophageal lumen. A small portion of this tissue was removed for histologic study. A 2d attempt to manipulate the nasogastric tube past this region was unsuccessful. Because of the possibility that

FIGURE 1. *X-Ray Film, Showing Complete Obstruction to Contrast Medium in the Lower Third of the Esophagus.*

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a congenital web was also present and because of our reluctance to resect this region in an infant, a small gastrotomy was performed on the herniated anterior gastric wall approximately 3 cm. distal to the cardia. A curved clamp

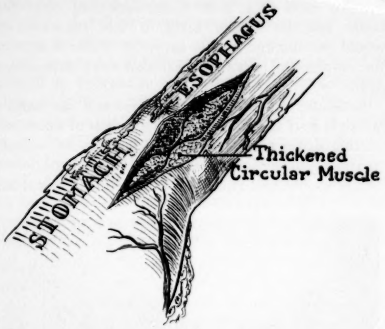

FIGURE 2. *Drawing, Showing the Relative Extent of the Myotomy and the Relations of the Encircling Muscle Band.*

was then inserted through the point of stenosis, and the cardia gently dilated by opening the jaws of the clamp (Fig. 3). The nasogastric tube was drawn down into the stomach, and the gastrotomy site closed. The esophagus was then mobilized almost to the level of the aortic arch and the diaphragmatic hernia repaired by a technique advocated by Humphreys.[1] Mattress sutures were placed circumferentially around the diaphragmatic hiatus 1 to 1.5 cm. from its edge, passing in the plane between diaphragm and peritoneum and through peritoneum, phrenicoesophageal ligament and seromuscular coat of the stomach just distal to the esophagogastric junction. The posterior suture was placed in such a manner that it included both rami of the hiatus (Fig. 4). When the sutures were tied, the hernia was reduced, and the hiatus narrowed (Fig. 5). An intercostal drain was inserted into the pleural space close to the site of the myotomy and connected to an underwater seal. The chest wound was closed in layers.

Postoperatively, the stomach was decompressed by intermittent nasogastric suction for 4 days. The chest drainage tube as well as the tracheostomy tube were removed on the

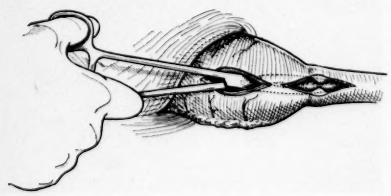

FIGURE 3. *Method Used to Dilate the Stricture.*

3d postoperative day. Oral feedings were started on the 4th day and were well tolerated thereafter. An esophagogram taken on the 14th day revealed an area of narrowing at the level of the diaphragm, with some delay in emptying of the proximal dilated esophageal segment (Fig. 6). Esophageal bougienage was carried out at weekly intervals, all bougies up to a No. 18 Fr. passing easily into the stomach. The baby continued to thrive and gain weight and was discharged 1 month after operation. Esophageal dilatations were continued in the outpatient department for 8 weeks, until a No. 28 Fr. bougie could be passed easily into the stomach. An esophagogram taken 8 months after operation revealed no obstruction (Fig. 7), and the baby has since continued to develop normally.

Microscopical examination of the tissue removed at operation and stained with hematoxylin and eosin, as well as by the Masson trichrome technic, showed hypertrophied muscle bundles separated by thin septa of fibrous tissue. There was evidence of low-grade inflammation, but the predominant picture was one of muscle hypertrophy rather than inflammation and fibrosis.

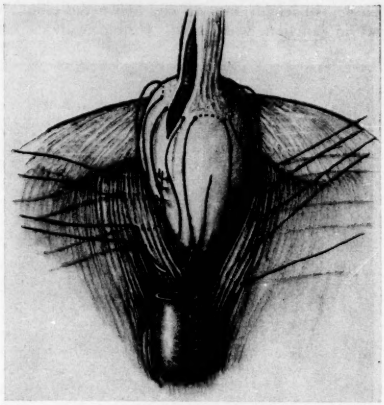

FIGURE 4. *Hiatus Hernia Viewed Posteriorly from above the Diaphragm, Showing the Method of Repair.*

DISCUSSION

Congenital obstruction of the esophagus by an annular band of hypertrophied or thickened muscle is a

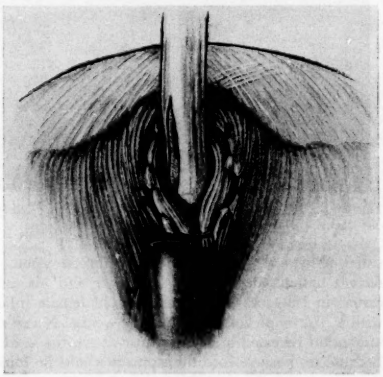

FIGURE 5. *Same View as Figure 4, Showing the Completed Repair.*

rare anomaly. Only 2 case reports similar to the 1 presented above were found in a review of the literature. In 1920 Ashby[2] described a patient with neo-

natal esophageal obstruction whose symptoms became pronounced when solid foods were started. Esophagograms revealed an area of stenosis 2.5 cm. above the diaphragm, and instrumental dilatation gave only transient relief. The child died at four years of age, having gained no weight in the preceding year and a half. At autopsy a well defined, thick annular band, 2.5 cm. in length and 2.5 cm. above the esophagogastric junction, was found. Histologically, it consisted of hypertrophied muscle and fibrotic tissue. A second patient, described by Holinger and his associates[3] in 1954, was a three-month-old female infant with a history of vomiting for nine weeks. X-ray examination revealed a stricture just above the cardia. Because no passage into the stomach could be found a gastrostomy was performed. Operation at six months of age disclosed a stricture consisting of "hard, gray-white tissue resembling in appearance, size and feel the tumor of congenital hypertrophic pyloric stenosis." A longitudinal incision was made through the stricture into the esophageal lumen and then closed transversely over a catheter. Symptoms were relieved though several dilatations were required over a period of nine months after the procedure. The authors made the interesting statement that they could find no similar cases in the literature and would recommend simple myotomy without entering the esophageal lumen if the lesion were encountered again.

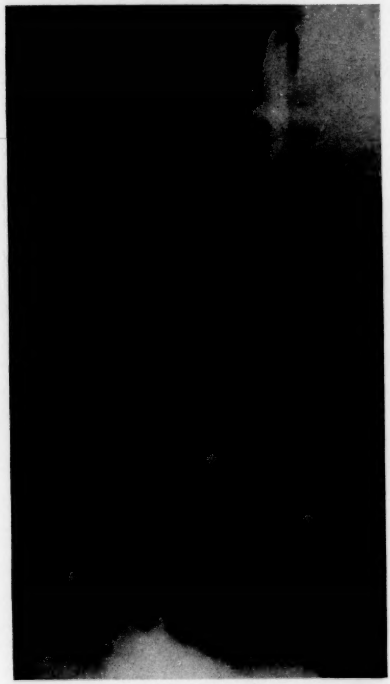

FIGURE 6. *Esophagogram on the Fourteenth Postoperative Day.*

Recently, Ingelfinger and Kramer,[4] as well as Schatzki and Gary,[5,6] reported a group of cases with varying degrees of dysphagia caused by an annular narrowing of the lower esophagus. They consider the "lower esophageal ring" to be a distinct clinical and pathological entity. The lesion was resected in 1 of the patients described by Ingelfinger and Kramer,[4] and microscopical examination of the excised specimen showed "extreme muscle thickening." Another patient included in the series reported by Schatzki and Gary was explored. The constricting annular ring was found to be at the level of the esophagogastric junction and was associated with a sliding hiatus hernia. Unfortunately, a biopsy failed to in-

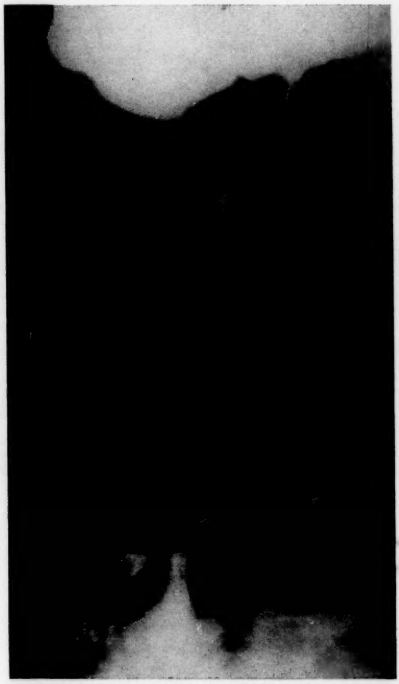

FIGURE 7. *Esophagogram Eight Months after Operation.*

clude muscularis, but the mucosa showed no inflammation. So far, the "lower esophageal ring" has been recognized only in adults. However, the nature of the obstructing lesion in the case reported above is so similar that it may well have represented a severe form of the same entity.

The origin of the hypertrophied muscle band is difficult to explain in the absence of a well defined anatomic circular sphincter at the cardia. The "collar of Helvetius,"[7] formed by circular and spiral muscle bundles of the esophagus reflecting to the left and right on to the stomach wall, may, according to Lerche,[8] contribute to a functional cardiac sphincter. An anomalous condensation and hypertrophy of these encircling muscle fibers might well explain the obstruction in this case. If this is true, it seems likely that a similar anomaly could occur at the cephalic end of the esophagus, where a comparable junction with other muscle groups occurs. Indeed, Johnson[9] described a case of annular muscle hypertrophy at the pharyngoesophageal junction in a twelve-year-old girl who had had symptoms of esophageal obstruction for nine years. Symptoms were completely relieved after a longitudinal myotomy was performed.

The cause of the muscle hypertrophy is obscure. Ashby[2] attributed the findings in his case primarily to muscle spasm with subsequent inflammation and fibrosis that he considered analogous to congenital hypertrophic pyloric stenosis. It is of interest, however, that in cases of neuromuscular dysfunction or achalasia in which the lower esophageal segment fails to relax, muscle hypertrophy is conspicuously absent. Moreover, in the reported cases, as well as in our own, symptoms began at birth, and it seems probable that the lesion is a true anomaly developing during intrauterine life.

The relation of the congenitally short esophagus to the lesion encountered in our case is also difficult to explain. Most authors agree that obstruction of the lower esophagus is somewhat more frequent among congenitally short esophagi, but obstructive symptoms usually do not develop in infancy. In the few cases that have been studied at autopsy or at operation, the obstruction has usually been the result of fibrosis secondary to reflux peptic esophagitis. In the case reported above, there was minimal evidence of esophagitis, and vomiting began as soon as an oral intake was started — two important points that argue for a true congenital stenosis. However, it is possible that the altered relations of the developing esophagus and phrenicoesophageal ligament modified the disposition of the muscular fibers of the so-called "collaris Helvetii," resulting in the abnormality.

Lesser degrees of esophageal obstruction caused by annular hypertrophic muscle at the cardia probably occur more frequently than is appreciated. Most of these cases are effectively treated by conservative bougienage, and the lesions are never directly visualized or palpated. Gross[10] reported three cases of stenosis at the cardia which were successfully treated by forceful dilatation. We have had experience with another patient in whom the roentgenographic and endoscopic findings were identical to those in the case reported above. However, a filiform leader could be passed endoscopically, and adequate dilatation carried out over a period of six months. When the obstruction is so severe that operative therapy must be undertaken, our experience, as well as that of Holinger and his associates,[3] suggests that conservative myotomy is the treatment of choice.

Summary

A case of esophageal stenosis at the level of the cardia associated with a congenitally short esophagus in a seven-week-old infant is presented. The obstructing lesion consisted of an annular band of hypertrophic muscle. Treatment by extramucosal myotomy combined with intralumenal dilatation is described. The possible origin of the circular muscle bundle is discussed.

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SPECIAL ARTICLE

RHEUMATIC HEART DISEASE IN THE FRAMINGHAM STUDY*

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THE pattern of distribution of rheumatic heart disease in the general population is of particular interest not only to those studying the natural history of rheumatic fever but also to those concerned with the pre-eminence of heart disease as a cause of disability and death. Studies of the epidemiology of rheumatic fever have helped to establish the association between that disease and streptococcal infections as well as to describe the familial aggregation of cases of rheumatic fever[1,2] and its predilection for northern latitudes.[3] However, data on the epidemiology of the late cardiac sequelae of rheumatic fever have been largely restricted to prevalence studies of valvular disease in children and young adults. The focus of attention in the older age groups has been upon the symptomatic phase of rheumatic heart disease, and little attention has been paid to the many asymptomatic patients with valvular deformities. Information about the entire clinical spectrum of rheumatic heart disease is of interest to the practicing physician since it will help him to manage the asymptomatic patient encountered in medical practice.

The cardinal statistic in the epidemiology of rheumatic heart disease is the over-all prevalence. Since this prevalence represents the number of individuals with rheumatic cardiac lesions per unit of population, the figure obtained depends not only upon the criteria used for the definitions of rheumatic heart disease, but also upon the kind of population to which these definitions are applied. Therefore, the true prevalence in the general population can be ascertained only by application of reliable and valid criteria of rheumatic heart disease to a representative sample of that population.

Previous data on the prevalence in adults have been obtained from autopsy figures, mortality and morbidity statistics, and clinical surveys of selected population groups.[4] Autopsy data[5] provide the most precise diagnosis of rheumatic heart disease but are usually derived from studies of hospital deaths, which represent a biased sample of deaths in the general population.[6] Mortality statistics have been shown to be unreliable because they are usually dependent upon the death certificate for the diagnosis of heart disease.[7] The majority of prevalence figures have been derived from periodic physical examinations of students,[8-10] Selective Service registrants[11] and other special groups.[12] Here, some care has been taken to establish reliably the clinical diagnosis of rheumatic heart disease. However, since most of the groups have been children, young adults or special occupational groups, with little attention to sampling technics, the figures obtained are difficult to relate to the other age groups or to the general population.

This study reports the over-all prevalence and some factors associated with the occurrence of rheumatic heart disease in 4494 persons from thirty to fifty-nine years of age examined in the Heart Disease Epidemiology Study, Framingham, Massachusetts.§

Although primarily concerned with hypertensive and arteriosclerotic heart disease, the Study afforded an extraordinary opportunity to establish the prevalence of rheumatic heart disease and to consider other factors associated with its occurrence in the population. Additional papers in preparation will report the prevalence of other etiologic types of heart disease.

METHODS

The Sampling Method

Framingham, Massachusetts, a town of about 30,000 population, lies 18 miles west of Boston. The population has a wide range of racial origin, occupation and economic status, and the age and sex distribution closely approximates that of the Commonwealth of Massachusetts and the United States as a whole. On January 1, 1950, a two-thirds random sample of the 9831 Framingham residents between the ages of thirty and fifty-nine was drawn, and the persons so chosen were invited to participate as subjects in the Heart Disease Epidemiology Study. Of the 6535 persons in the sample drawn 4494 (68.8 per cent) were examined between January, 1948, and March, 1953, and constitute the group upon which this study is based.¶

Clinical Methods

Examination. Each subject received a detailed

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§The Framingham Study, conducted by the United States Public Health Service in co-operation with the Massachusetts Department of Public Health, was established in 1948 as a twenty-year study of many factors related to the development of heart disease in a representative sample of the population.[13]

¶Statistical analysis of these data was performed by the Biometrics Research Section of the National Heart Institute under the supervision of Mr. Felix E. Moore and with the technical assistance of Miss Dorothea M. McElholm.

cardiovascular examination, of which the following features related specifically to the diagnosis of rheumatic heart disease:

History

The subjects were questioned by a physician about whether or not they had experienced rheumatic fever, "growing pains," chorea or painful or swollen joints. On a standard form the physician then recorded his opinion of whether or not he believed that the history indicated rheumatic fever. Subjects with symptoms of rheumatic disease were requestioned by a second physician.

Physical examination

Each subject received a detailed physical examination of the heart by two physicians, each of whom recorded his findings independently. When marked differences occurred, particularly regarding auscultatory findings, the two physicians either re-examined the subject together or called in a third physician to resolve differences.

X-ray examination

A 14-x-17-inch teleroentgenogram, with a target distance of 80 inches, was taken on each subject and was interpreted by consultant radiologists with particular attention to generalized enlargement of the heart, specific chamber enlargement, or abnormal cardiac contour. In addition, many subjects with murmurs or x-ray evidence of rheumatic heart disease were fluoroscoped in an effort to demonstrate left auricular enlargement.

Electrocardiogram

A 12-lead electrocardiogram, including standard leads 1, 2 and 3, unipolar leads aVR, aVL and aVF and V_1 through V_6, was recorded from each subject and interpreted by staff physicians. Doubtful or abnormal tracings were sent for special interpretation.

Criteria for Diagnosis of Rheumatic Heart Disease

The criteria used for the definitions of rheumatic heart disease were based upon the recommendations of the New York Heart Association,[14] and the grading of heart murmurs was modeled after Levine's[15] classification. The main criterion was auscultatory evidence of valvular disease, but when murmurs of borderline intensity raised doubts, a history of rheumatic fever was used as an additional criterion. However, in some subjects the diagnosis remained indefinite, and these cases were classed as "possible rheumatic heart disease."

TABLE 1. *Prevalence of Rheumatic Heart Disease by Age and Sex.*

Age Group	Population			Cases of Rheumatic Heart Disease			Prevalence		
	TOTAL	MALE	FEMALE	TOTAL	MALE	FEMALE	TOTAL	MALE	FEMALE
yr.							*per 1000*	*per 1000*	*per 1000*
30-39	1612	730	882	39	11	28	24	15	32
40-49	1496	673	823	42	15	27	28	22	33
50-59	1386	633	753	40	21	19	29	33	25
Totals (30-59)	4494	2036	2458	121	47	74			
Averages							27	23	30

Specifically, the definitions of rheumatic heart disease that were applied to the sample were as follows:

Definite rheumatic heart disease

Any diastolic murmur in the mitral or aortic area in the absence of other known types of heart disease (for example, congenital or syphilitic) was considered definite evidence of rheumatic heart disease.

TABLE 2. *Distribution of Valvular Lesions by Type and by Grade of Rheumatic Heart Disease.*

Type of Lesion	No. of Cases of Rheumatic Heart Disease						Distribution (All Grades)
	ALL GRADES		DEFINITE		POSSIBLE		
							%
Mitral valve only	62		41		21		51.2
Mitral stenosis	28		28		—		
Mitral insufficiency	28		7		21		
Mitral stenosis & mitral insufficiency	6		6		—		
Aortic valve only	25		19		6		20.7
Aortic stenosis	6		—		6		
Aortic insufficiency	17		17		—		
Aortic stenosis & aortic insufficiency	2		2		—		
Multiple valvular involvement	34		31		3		28.1
All types	121		91		30		100.0

A Grade 4 systolic murmur in the mitral or aortic area, with or without a history of rheumatic fever, or a Grade 3 murmur with a history of rheumatic fever was considered to be evidence of definite rheumatic heart disease.

Possible rheumatic heart disease

A Grade 3 mitral or aortic systolic murmur in the absence of a history of rheumatic fever or a Grade 2 plus systolic murmur in the same areas, together with a history of rheumatic fever, was defined as possible rheumatic heart disease.

Results

Prevalence of Rheumatic Heart Disease

A hundred and twenty-one of the 4494 subjects examined fulfilled the criteria for the diagnosis of rheumatic heart disease. This represented a prevalence of 27 per 1000 (Table 1). The remaining 4373 subjects were judged to be free of rheumatic heart disease and served as a comparison group for many of the observations.*

Among the men in the sample there was an increase in prevalence with age of marginal significance ($0.10>P>0.05$), from 15 per thousand in the decade thirty to thirty-nine years to 33 per thousand in the decade fifty to fifty-nine years. In women the prevalence was slightly higher, but cases were distributed evenly by decade. It is also of interest that in the youngest decade studied, rheumatic heart disease was twice as prevalent in women as in men ($0.05>P>0.02$).

The type of valvular involvement and the grade of rheumatic heart disease in the 121 subjects are shown in Table 2. In 62 subjects (51.2 per cent of the total with rheumatic heart disease) the involvement was of the mitral valve alone; 28 of these had "pure" mitral stenosis. Of 25 (20.7 per cent) considered to have isolated aortic-valve involvement, 17 had "pure" aortic regurgitation. The remaining 34 (28.1 per cent) had the murmurs indicating multiple valvular disease. According to the criteria used, 91 (75.2 per cent) of those examined were believed to have unequivocal evidence of rheumatic heart disease whereas another 30 (24.8 per cent), most of whom exhibited the murmur of mitral insufficiency, belonged to the borderline group designated as possible rheumatic heart disease.

Isolated mitral-valve involvement was almost three times as prevalent among women as among men ($P<0.01$). Although aortic-valve involvement alone was almost twice as prevalent among men as among women, this difference was not significant ($0.15<P<0.2$), and multiple involvement was distributed about equally between the two sexes (Table 3).

There was little functional incapacity among the subjects with rheumatic heart disease (Table 4). The conditions of the examination itself excluded any bed-ridden patient with cardiac disease (Class 4†), and only 1 patient was classified as severely restricted (Class 3). Sixteen others were believed to have little incapacity (Class 2), and 104 had no restriction (Class 1) of activity at the time of examination.

TABLE 3. *Distribution of Valvular Lesions by Sex in Subjects with Rheumatic Heart Disease.*

Type of Lesion	No. of Cases			Rate per 1000 Examined		
	Total	Male	Female	Total	Male	Female
Mitral valve only	62	14	48	14	7	20
Mitral stenosis	28	8	20			
Mitral insufficiency	28	6	22			
Mitral stenosis & mitral insufficiency	6	—	6			
Aortic valve only	25	15	10	6	7	4
Aortic stenosis	6	3	3			
Aortic insufficiency	17	11	6			
Aortic stenosis & aortic insufficiency	2	1	1			
Multiple involvement	34	18	16	8	9	7
All types	121	47	74			
Average				27	23	30

Other Pertinent Findings Associated with the Presence of Rheumatic Heart Disease

Other studies have shown that less than half the patients with rheumatic heart disease are able to recall clinical manifestations of rheumatic fever. Since the present study established a history of rheumatic fever as one criterion in the diagnosis of rheumatic heart disease, only patients in whom the diagnosis was based upon auscultatory findings alone (that is, the presence of a diastolic murmur) were analyzed regarding a past history of rheumatic fever (Table 5). Of this group, 35 (41.7 per cent) recalled having had rheumatic fever, but this varied from 54.8 per cent of those with multiple valvular involvement

TABLE 4. *Functional Status of 121 Subjects with Rheumatic Heart Disease.*

Status*	No. of Cases	Distribution
		%
Functional Class 1	104	86.0
Functional Class 2	16	13.2
Functional Class 3	1	0.8
Functional Class 4	—	—

*Classification of N. Y. Heart Association.[14]

*It should be emphasized that this comparison group included persons with heart disease of other than rheumatic etiology.

†Functional capacity based on classification of the New York Heart Association.[14]

to 21.1 per cent, with aortic regurgitation alone. Rheumatic fever was apparently twice as common in subjects with mitral stenosis as among those with aortic regurgitation, and this difference could not be explained by the older average age of subjects with aortic lesions in whom more time had elapsed since the last attack of rheumatic fever.

To determine whether or not the subject was aware that he had valvular disease each subject was asked if he had ever been told by a physician that he had a heart murmur. Table 6 reveals that less than half (43 per cent) of those with rheumatic heart disease were aware that they had a heart murmur before examination in the Framingham Study. As might have been suspected this finding correlated with the prior knowledge of rheumatic fever, since 64.1 per cent of subjects with a history of rheumatic fever were aware that they had a heart murmur, whereas only 28.9 per cent of those without such a history knew that they had valvular disease. It is also of interest that almost 1 out of 10 subjects in the comparison group (8.9 per cent) without evidence of rheumatic heart disease had been advised of the presence of a heart murmur by a physician at some time before the Framingham examination.

Table 7 summarizes other pertinent findings in the subjects with and without rheumatic heart disease. A history of rheumatic fever and frequent sore throats were both somewhat more frequent among the former than among the latter. The x-ray film was interpreted as showing generalized or specific chamber enlargement of the heart in less than half (47.9 per cent) of those with rheumatic heart disease, and over a quarter (25.9 per cent) of the comparison group were believed to have some heart enlargement with the use of the same sensitive x-ray criteria. Doubtful or abnormal electrocardiograms were present in 27.3

TABLE 5. *History of Rheumatic Fever in Subjects with Rheumatic Heart Disease by Type of Valvular Lesion.**

TYPE OF LESION	NO. OF CASES			PERCENTAGE WITH HISTORY OF RHEUMATIC FEVER
	TOTAL	WITH HISTORY OF RHEUMATIC FEVER	WITHOUT HISTORY OF RHEUMATIC FEVER	
Mitral stenosis	34	14	20	41.2
Aortic regurgitation	19	4	15	21.1
Mitral stenosis & aortic regurgitation	31	17	14	54.8
All types	84	35	49	
Average				41.7

*Includes only subjects with diastolic murmurs since history of rheumatic fever represented only criterion for diagnosis of rheumatic heart disease in subjects with borderline systolic murmurs.

TABLE 6. *Subjects with Rheumatic Heart Disease with a History of Heart Murmur by Type of Valvular Lesion.*

TYPE OF LESION	NO. OF CASES			PERCENTAGE WITH HISTORY OF HEART MURMUR
	TOTAL	WITH HISTORY OF HEART MURMUR	WITHOUT HISTORY OF HEART MURMUR	
Mitral valve only	62	26	36	41.9
Aortic valve only	25	6	19	24.0
Multiple	34	20	14	58.8
All types	121	52	69	
Average				43.0

TABLE 7. *Comparison of Other Pertinent Findings in Subjects with and without Rheumatic Heart Disease.**

FINDING	NO. OF SUBJECTS		PERCENTAGE WITH SPECIFIED FINDING
	EXAMINED	WITH SPECIFIED FINDING	
History of rheumatic fever:			
Subjects with rheumatic heart disease	121	52	43.0
Subjects without rheumatic heart disease	4373	218	5.0
History of heart murmurs:			
Subjects with rheumatic heart disease	121	52	43.0
Subjects without rheumatic heart disease	4350	389	8.9
History of scarlet fever:			
Subjects with rheumatic heart disease	121	32	26.4†
Subjects without rheumatic heart disease	4313	821	19.0
History of frequent sore throat:			
Subjects with rheumatic heart disease	121	38	31.4
Subjects without rheumatic heart disease	4313	832	19.3
X-ray evidence of heart enlargement:			
Subjects with rheumatic heart disease	121	58	47.9
Subjects without rheumatic heart disease	4346	1126	25.9
Electrocardiographic abnormalities‡:			
Subjects with rheumatic heart disease	121	33	27.3
Subjects without rheumatic heart disease	4371	442	10.1

*Variations in number of subjects without rheumatic heart disease due to incomplete testing of all subjects.

†All differences between subjects with & without rheumatic heart disease statistically highly significant ($P<0.01$) with exception of history of scarlet fever, in which case less than 1 chance in 20 ($P<0.05$) that difference due to chance alone.

‡Tracings of 5 persons with & 12 without rheumatic heart disease gave evidence of atrial fibrillation.

per cent of the rheumatic subjects, but 10.1 per cent of the nonrheumatic subjects showed some abnormalities. In only 5 (4.1 per cent) subjects with rheumatic heart disease did the cardiac rhythm show atrial fibrillation at the time the tracings were recorded.

A history of rheumatic disease among parents, siblings and children of subjects with rheumatic heart disease was recorded and compared with a smaller matched group of 121 subjects of similar age and sex distribution. A family history was somewhat more common in the former, but the differences were small and not statistically significant. The same matched group was used for analysis of a history of "growing pains" in childhood, and evidence of freckling. In neither case was a significant difference present.

Discussion

The age and geographic distribution of the sample chosen for the study were arbitrarily limited because of the primary interests of the Framingham Study. In addition there are reasons to believe that the distribution of rheumatic heart disease was not exactly the same among those examined as among those who declined examination. Some persons selected died of rheumatic heart disease before the initial examination, and others were hospitalized or were otherwise too sick to accept examination. However, since the selection of the sample there have been 4 deaths from rheumatic heart disease (between January, 1950, and October, 1955) in the nonco-operating group, as compared with 7 deaths among those examined; this experience suggests no significant difference in death rates from rheumatic heart disease between the two groups since the examined group was twice the size of the group not examined. Efforts are being made to get more information, through careful study of the cause of death, about the cardiac status of those who refused examination.

The criteria used in the definitions of rheumatic heart disease were necessarily arbitrary and contained the inaccuracies inherent in the use of auscultatory findings as a true measure of valvular deformity.

At the time of the second examination approximately two years later, of the 121 subjects with rheumatic heart disease, 4 were dead, 9 refused examination, and 108 returned for re-examination. Of these 108 subjects 20 (18.5 per cent) no longer fell within the diagnostic criteria for rheumatic heart disease. On the other hand a new diagnosis was made on 25 subjects initially included in the nonrheumatic group. It is impossible at present to tell how many of the 13 subjects who lost diastolic murmurs and the 11 subjects in whom diastolic murmurs developed during the two-year period represent the inability of the examining doctors to hear the murmurs and how many represent the true changes in valvular deformity that have been observed during previous follow-up studies of patients with rheumatic fever.[16,17] It should become easier to differentiate the true valvular changes from auscultatory errors as the subjects are followed over a twenty-year period in the Framingham Study.

The over-all prevalence of rheumatic heart disease of 27 per 1000 is somewhat higher than that found in most other studies[4,18] and probably represents special care in examination and more sensitive criteria for diagnosis. Even if subjects with possible rheumatic heart disease are excluded, the prevalence rate (20 per 1000) is still in excess of previous experience. In addition, since geographic differences have been shown to influence the occurrence of rheumatic heart disease,[3] it is possible that the prevalence of this disease is somewhat higher in Framingham than in other areas within the United States.

The curious predominance of mitral-valve deformity in women is not unique in this study.[15] This excess seemed evenly distributed throughout the three age decades studied. In males the increase in prevalence of rheumatic heart disease with age apparently was due to the development of aortic stenosis and regurgitation. However, since only 4 of the 19 patients with aortic regurgitation gave a history of rheumatic fever, it is possible that some of these aortic lesions represented other types of heart disease.

The functional classification emphasizes that the rheumatic subjects were very little disabled by their heart disease. In addition most of the subjects were not aware that they had heart murmurs before the Framingham examination. This was particularly true of those with aortic insufficiency, as might have been predicted, since this murmur is the most difficult to identify under the usual circumstances of a physical examination.[19]

In view of the relatively mild nature of the majority of rheumatic valvular deformities found, it is not surprising that less than half the subjects with rheumatic heart disease showed abnormalities on a standard posteroanterior x-ray film of the chest. Many of these subjects probably had a minimal degree of enlargement of the left atrium that could have been determined by careful fluoroscopic examination. However, since fluoroscopic study of each subject was not possible, such enlargement was not included as a diagnostic criterion of rheumatic heart disease.

The large number of rheumatic subjects with a normal cardiac silhouette, combined with the high proportion of others in the sample with x-ray evidence of cardiac enlargement, should discourage those interested in using this test as an isolated screening procedure for the identification of persons with rheumatic heart disease. Similarly, the electrocardiogram was recorded as abnormal from only 1 person with rheumatic heart disease out of 4 and, therefore, also represents a relatively insensitive screening technic.

Previous epidemiologic studies have indicated more streptococcal disease in rheumatic patients and familial aggregation of rheumatic fever.[20] Also, it has been suggested that "growing pains" represent a subclinical manifestation of rheumatic disease, and that rheumatic fever is more common among persons with marked freckling of the skin.[15] This study shows that histories of frequent sore throats and scarlet fever are more common among the rheumatic than among the nonrheumatic group; however, this difference may mean only that patients with rheumatic heart disease were aware of the relation between streptococcal infections and rheumatic fever rather than a truly increased prevalence of these infections among rheumatic subjects. The data on family history are in the expected direction, but inconclusive. It appears that a history of "growing pains" does not accurately reflect subclinical rheumatic fever in childhood and that rheumatic heart disease is not more common in persons with freckles than in others.

Summary

The prevalence of rheumatic heart disease in 4494 persons selected at random from a population between thirty and fifty-nine years of age in Framingham, Massachusetts, was 27 per 1000.

Mitral-valve involvement was almost three times as prevalent in females as in males.

Of those 121 subjects with rheumatic heart disease 86.0 per cent had no functional impairment at the time of examination.

Observations on other pertinent factors concerning the epidemiology of rheumatic heart disease are reported.

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MEDICAL PROGRESS

PHYSICAL MEDICINE AND REHABILITATION

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TO those interested in the field of physical medicine and rehabilitation the major sources of publications in this country are the *Archives of Physical Medicine and Rehabilitation*, the *American Journal of Physical Medicine* and the *Physical Therapy Review*. In addition, of course, articles appear in the various specialty journals, all of which are now interested in rehabilitation and present papers of interest to specialists in physical medicine (physiatrists) as well as specialists in their own fields. The present review of literature in recent years is devoted to selections of certain articles found in these journals and also those representing presentations in the *Journal of the American Medical Association* in which the Section proceedings at annual meetings are published, as well as some of the specialty journals such as the *Archives of Neurology and Psychiatry*, the *Journal of Bone and Joint Surgery* and *Geriatrics* and other closely allied fields. No attempt has been made to cover the literature completely. Only articles thought to be of interest to those either specializing in physical medicine or in general practice will be considered.

There still appears to be a need for more up-to-date textbooks in this rapidly changing field. A volume prepared in 1951 from the Mayo Clinic under the editorship of Frank Krusen and entitled "Physical

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Medicine and Rehabilitation for the Clinician"[1] is one of the best general presentations of articles by many specialists in the field. One of the newer textbooks, and presumably one of a series to follow, concerns electrodiagnosis and electromyography and appeared in recent months.[2] Most of the older works are somewhat outmoded, and up-to-date information must be obtained from the current literature. The last review in this series was entitled "Current Trends in Physical Medicine and Rehabilitation," and since then other papers have appeared with similar titles.[3] For example, it appears that the specialty board, which has been in existence for nine years, during the course of its development became a leader in the field of directing the training of physicians in physical medicine and rehabilitation so that they would develop special skills for treating patients to attain maximum rehabilitation in spite of various physical disabilities. Despite this specialization in training, general interest has spread to all areas of medical practice. Many other specialties have believed that the rehabilitation technics are better taught within their own training program, and in view of this the American Medical Association has taken away the term of "rehabilitation" from the specialty of physical medicine. This has the advantage of interesting more physicians in this important aspect of the practice of medicine. Knowledge of technical details and leadership seem to be remaining, however, in the field of physical medicine.[3]

Electrodiagnosis

In the specialty of physical medicine the technics of electrodiagnosis have continued to be developed on the research and clinical level. The background of electrodiagnosis is ancient, as all neurologists and physiologists well know. Clinical applications have, to a large extent, been developed in the hands of physiatrists and neurologists, and most of the recent articles summarizing the present standing of electrodiagnostic measures appear in the publications of the physical-medicine journals.[4] In summary, determination of rheobase, chronaxie and a more thorough study of the excitability as indicated by strength-duration curves remain the fundamental methods of measuring lower-motor-neuron function. The reference to faradic response is now archaic because such currents are actually not utilized, although physiologically similar currents are used and determine the same important information — namely, the excitability threshold of tetanizing currents where the individual impulse is of short duration. One can say that the rheobase determinations are of some importance, as well as the chronaxie. More quantitative still are the strength-duration curves of electric excitability. Observation of the type of response is still of clinical value — that is, whether the response is brisk or sluggish or whether there is a difference between the polar responses. No particularly new information has been recorded, however, in this regard in recent years, although the literature has clarified some of the clinical details.[4]

Utilization of electromyography has come to the fore in electrodiagnostic technics. It is my opinion that electromyography interpretation is of more importance than description of actual electric potentials recorded. This is due to the fact that there are still no generally accepted standards of technic of recording as in electrocardiography. To be of significant importance the electromyograms must accordingly be done by a physician using intramuscular needle recordings. There must be accurate observation of the condition of the patient, particularly his relaxation or positioning throughout the period of observation. In the hospital clinic one finds that requests are made for electromyographic recordings when no valuable information can be obtained from the tests. In actual practice the electrodiagnostician must determine for himself whether measurements of electric excitability by quantitative measures are more important than electromyography or where the combination of the two gives the desired information.

In brief it can be stated that the present electrodiagnostic tests are of most value in determining the presence or absence of lower-motor-neuron disease or injury. Upper-motor-neuron lesions can better be distinguished by clinical than by electric tests with the possible exception that hysterical reactions can be detected by electric tests in some cases.

Biophysical Aspects of Physical Medicine

Radiation and Diathermy

One subject of particular interest in the field of physical medicine has been the relative effectiveness of different types of electric energy in heating superficial and deep tissues. Previous studies have included the relative depth penetration of radiant energy in both the visual and infrared areas and the depth of heating produced by high-frequency electromagnetic energy commonly called diathermy. A recent study by Martin and Herrick,[5] of the Mayo Clinic, was done to determine the relative heating effects of infrared radiation as used clinically when compared with microwaves that have a frequency of 2450 megacycles (commonly known as microwave diathermy). It was found that microwave diathermy consistently raised the temperatures in the muscles of the thigh to levels of more than 104°F. (40°C.) when applied for twenty minutes with the usual clinical technics and dosages. Infrared radiation failed, however, to produce significant elevations of temperature at a depth of 5 cm. from the skin surface. It was concluded, therefore, that microwave diathermy is an effective method for heating muscle tissues at deep levels according to usual clinical practices in human beings.

Another important view of this subject of deep heat by electric energy has recently appeared from

Philadelphia by Schwan,[6,7] whose papers consider the biophysical basis of physical medicine. In these articles the previous literature on the effects of diathermy and radiation are summarized, with some reference also to ultrasound therapy. It has been pointed out that important aspects in the use of diathermy are to differentiate selective, structural and volume heating. They indicate that it has been impossible to heat selectively volume fractions smaller than 1 cu. mm. This suggests that selective heating of bacteria and like objects is impossible. Careful studies have shown that both ultrasonic therapy and microwave diathermy have greater depth effect than so-called short-wave diathermy. These excellent papers indicate that for depth of penetration in deep tissues of muscular type, with the usual technics and dosages, the use of ultrasonic equipment is favored. Presently available microwave equipment is capable of delivering effective energy to tissues with high water content when the subcutaneous fat layers are rather thin. Clinically, there are certain advantages in the use of microwave therapy, for the upper energy level where irreversible damage to tissue can occur is higher than with ultrasonic radiation and the margin between minimal effective dosage and maximum permissible dosages is greater than in the use of ultrasound. Microwaves in certain areas, as in the treatment of joints, it is pointed out, are also preferable to ultrasonic energy. The important fact has repeatedly been emphasized that dosage cannot be read simply by meters, whether diathermy or ultrasound is used, and special care must be taken in the use of ultrasound, for the margin of safety between effective and injurious dosage is narrow. The various physical factors involved are well described and are of interest to those dealing in this specialty of physical medicine.

Ultrasound

Perhaps the most talked about new physical agent in physical medicine is ultrasonic radiation. The *American Journal of Physical Medicine* has devoted an entire issue to this subject,[8] indicating that many physicians are greatly appreciative of the therapeutic values of ultrasonics in medicine. This is further suggested by the fact that the former Council on Physical Medicine and Rehabilitation of the American Medical Association has presented an article indicating that there are definite benefits of this type of therapy and listed the main indications and contraindications.[9] There is also a chapter devoted to the subject in a current textbook.[10]

As is true of the majority of physical agents used in the field of physical medicine it is impossible to set up accurate control studies in which the value of a single physical agent can be determined. Everyone concedes that ultrasonic energy is a method that is quite effective in producing deep heat in tissues when applied according to the recommended technics and dosages. Most authors agree that whenever deep heat is indicated therapeutically, ultrasonic energy may be considered an effective method for this purpose. Experimental studies have suggested that there may be some specific effects of ultrasonic energy on certain tissues, particularly nerve tissues and at interfaces of deeply situated structures. There is also some theoretical evidence that there may be some other effect than deep heating because of the unique mechanical action of this type of energy. There may be, for example, a type of "micromassage" that future studies may suggest to be of therapeutic value. Destructive mechanical effects, such as cavitation, have been described with overdosage. There is no evidence, however, of any late deleterious action of the type produced by large dosages of x-rays.

In summary it can be stated that ultrasonic energy can be a very powerful form of deep heating and may produce some other effects not yet well understood. There appears to be no evidence from a physical basis that it has any long lasting effects, such as that produced by irradiation with x-rays. In general the same precautions that apply to the use of diathermy and microwave diathermy apply to the use of ultrasonic energy. It has certain advantages in that it is generally applied by the physician, who can determine its effect at the time, and the dangers of overdosages are accordingly diminished as long as the physician knows the characteristics of the energy he is applying therapeutically.

Apparatus

The development of various mechanical aids to assist handicapped people is of great concern to those in the field of rehabilitation. A considerable body of literature has already been assembled by various agencies and is made available to all those in the field.[11] This describes varieties of self-help devices to aid in the activities of daily living and also devices to make it possible for the severely paralyzed to have useful hobbies and, at times, occupations. This equipment has been developed primarily for the severely paralyzed patient with poliomyelitis,[12] the crippled arthritic patient and the patient with traumatic quadriplegia. Of special interest is the still experimental development of devices to increase the use of the upper extremities in the completely, or almost completely, paralyzed patient by means of exoskeletal prostheses and similar devices.[13] At present development has not reached the stage where the devices can be obtained commercially for the average patient without an adaptive-equipment machinist available, for most of the apparatus has to be custom made for the patient.

A report of interest is that of the effect of a new mechanical device producing centripetal rhythmic compression on localized edema of an extremity. Wakim and Krusen,[14] of the Mayo Clinic, have shown that this device has been effective in reducing

the swelling and edema from chronic lymphatic obstruction, as in postradical mastectomy. This new type of vasopneumatic apparatus works automatically and may have other uses for relief of chronic edema.

Exercise Physiology and Technics

Although in the past the chief interest of those in physical medicine may have been in the development of the application of various powerful physical agents in therapeutics the emphasis has now tended to shift more to studies of exercise physiology and improvements in therapeutic-exercise technics. During the past five years a major change has been occurring in the technics of exercise in overcoming paresis. The traditional method in the past has relied on rest and gradual increase in activity, with avoidance of fatigue. Routine progression in treatment was from passive motion to assistive and free motion and, finally, to motion against gravity, followed by resistive exercise. Careful isolation of motion to individual muscles and avoidance of stretch have been emphasized. The first step away from this more conservative approach to muscle re-education was the use of progressive-resistance exercise with loads up to the maximum for the individual muscle groups exercised. This is a method of few repetitions and heavy-resistance exercise.[15]

Newer methods have been developed largely at the Kabat-Kaiser Institute in Vallejo, California, under Dr. Herman Kabat and Margaret Knott and their various associates, who have since then been trained in the methods. This exercise technic is based on a program of manual resistive exercises. Efforts are made to facilitate muscle contraction by stretching and exerting maximum resistance. Attempts are made to utilize fundamental movement patterns carried out against manual resistance with appropriate stretch of the muscles preceded or followed by reversals of the antagonists in the pattern. The specific movement pattern is performed through the range of motion until fatigue is quite evident by decreased response. The pattern is then taken over to the antagonists for restoration of power through the facilitation thus obtained. It has been the experience of those advocating this method that only minimal rest is necessary to recover from fatigue and that reversal of pattern almost immediately brings about the desired result when the original motion may be repeated. In summary the essence of this re-education technic is based on maximal resistance, stretch, fundamental movement patterns, proprioceptive and reciprocal reflexes and reversal of antagonists. In actual practice the exercises are carried out for a number of hours each day, fatigue being disregarded as much as possible, in comparison with the fifteen or twenty minutes once or twice a day — the usual physical-therapy treatment.

The technics of this proprioceptive facilitation are based on the works of Sherrington and others on the functioning of reflex centers and are becoming more and more accepted clinically. These methods have been applied to a variety of clinical conditions, particularly poliomyelitis, multiple sclerosis and other chronic neurologic disorders, rheumatoid arthritis and muscle weakness from disuse of many causes. So far, critical comparison of these methods with others previously used has been difficult. There can be little doubt, however, from my experience that the physical therapists who have learned the technic and who judge results from their own subjective feeling of increasing strength in the patient believe that these technics are more helpful than others previously used. In my experience, also, the patients believe that they get more out of their exercise program when these methods are employed. In the analysis of results, however, it should be pointed out that these technics take much more of the individual therapist's time in treating the patient and take advantage of the psychologic factor of the close contact during manual resistance over a more-or-less prolonged period. Psychologically, this may be a great satisfaction to the patient who is severely handicapped and who receives several hours of personal treatment daily as compared with a much shorter time under conventional technics. In spite of these factors it is my opinion that a new important advance has been made in neuromuscular re-education. Fortunately, for those interested in this subject a textbook by Knott and Voss,[16] two expert physical therapists, has just appeared; the descriptions and illustrations are excellent.

Clinical Applications in Physical Medicine

Cerebrovascular Accidents (Hemiplegia)

The treatment of the hemiplegic patient who has suffered a cerebrovascular lesion, either thrombosis or hemorrhage, and survives is aimed at obtaining maximum recovery by whatever means are available. In general it can be stated that the younger the patient, the better the results, other things being equal.[17] This is probably due to a number of factors, including the degree of generalized vascular disease present in the older patient that causes brain damage so that he is not susceptible to treatment. It has also been observed that the younger patients are more willing to accept their disability and work with the remaining abilities to compensate for the permanent handicap as compared with the older person, who concentrates only on the disability and with difficulty learns any new methods of doing things for himself or in work.

The immediate care of the hemiplegic patient who has suffered a cerebrovascular accident has been well described by neurologists and internists and need not be reviewed here. This is also not the place to discuss in detail the value of sympathetic blocks, cortisone and anticoagulants or other medicinal treatment. Emphasis is on the physical treatment, which at first is largely that of proper nursing care.[18] Deformities of the hand and leg can be prevented by

splinting and exercise. Much of it can be carried out with the help of well instructed relatives or assistants to the family. In general one of the primary aims is to regain the power of ambulation. First, one may begin with bed exercises, including sitting exercises later, with emphasis on trunk balance. Much of the success of ambulation depends on re-education of balance, which can be started at an early date while the patient is still in bed. The natural progress of treatment is, of course, to standing with aids, such as parallel bars and consideration of bracing, which is often necessary for the lower extremity.

The problem of aphasia and loss of the use of the dominant upper extremity is difficult to face, especially for the older patient. One so often sees a great degree of spontaneous improvement in language ability that the role of special speech therapy is difficult to evaluate. Certainly, stimulation of language function is to be encouraged at the proper time in all patients. Records have shown that, particularly in the younger patients, specialized technics in speech therapy seem to have very valuable results.[19] One of the difficult problems has been in determining whether an end point in therapy has been reached or whether a permanent residuum, particularly of the upper extremity, is to be accepted in many cases. It is difficult for the older patient with set personality to accept the paralysis of his dominant hand, for example, and he will continually search for treatment or for miraculous cures. The end results regarding return to employment, as might be expected, are much more favorable in my experience in the younger patients. Exceptions are notable, however, and all efforts should be made to evaluate the patient thoroughly from a point of view of physical capabilities, prognosis of the general cardiovascular condition and also the degree of cerebral damage and deterioration of intellectual functions.

Arthritis and Other Chronic Diseases Especially of Old Age

Over the years much has been written concerning use of physical agents such as heat in various forms, occasionally massage, hydrotherapy and therapeutic exercises in the treatment of the patient with rheumatoid arthritis.[20] All these methods are still an essential part in the treatment of these patients, including, also, occupational therapy, when available, to assist the patient in maximum self-independence. It has to be realized, however, that none of these physical therapeutic measures are curative, being only adjuncts to the general treatment. Emphasis is to be placed, however, on the total rehabilitation of these patients by all available means that have been developed in recent years. An interesting study — and an informative one — was recently made and reported by Lowman, Lee and Rusk,[21] who pointed out the need of combination of any available specific, or nearly specific, methods of treatment with their total rehabilitation program. They concluded that the ideal subject for rehabilitation is a patient with a burned-out, or quiescent, case in whom control of the pathologic process has been accomplished; they represent static disability and are able to take advantage of mechanical aids to the fullest extent. At the same time the psychologic factors must be carefully worked out, and it has been pointed out that it is essential that the patient have proper motivation if the goals of rehabilitation are to be obtained. It is also recommended that specific and realistic goals be set up for the patient, and the factors that lead to establishing prognosis have been studied, particularly regarding the past history of the individual patient. This study also shows in detail some of the adaptive equipment that can be of value to some of these patients and the importance of team co-operation in the treatment program.[21]

In considering the treatment of the elderly patient, including those with chronic diseases other than arthritis, Ferderber et al.[22] have pointed out the importance of having available physical therapeutic methods, occupational therapy and again a team approach so that all specific medical care can be employed together with the physical rehabilitative measures that have been shown to be of value. Advantages of group activity and physical activity in general have been emphasized repeatedly, together with the need of adequate socialization and recreation. There also seems to be a need of education of families to teach them the proper management of the elderly patient within the home. (The reader is referred to *Geriatrics* for detailed information.)

Paraplegia

The rehabilitation of the paraplegic patient has been a subject of widespread medical interest, particularly since World War II, as the length of life of these patients has increased primarily through development of methods in controlling urinary-tract infection and function and other complications of metabolism. Contributions to this important subject have been presented in Munro's[23] book and in various articles that have appeared in this journal.[24] Experience in the Veterans Administration hospitals has also led to a fund of knowledge that is available to those treating these patients in special articles in technical bulletins dealing with the physical rehabilitation of the patients. No detailed reference to this widespread literature need be made here. A report, however, that may be of particular interest to the internists deals with the subject "Metabolism in Paraplegia" by O'Connell and Gardner.[25] Another subject often overlooked in the care of the paraplegic patient concerns emptying of the bowel and is worthy of careful study.[26]

The methods of physical rehabilitation of the paraplegic patient, including bracing and exercise and gait training, have been outlined in book form and

are very helpful to those dealing with this rehabilitation technic.[27] A recent study indicates that, although many patients can be taught to ambulate for short distances with crutches and braces, perhaps a majority, because of the necessary great physical exertion put upon them, cannot be expected to ambulate on crutches and braces at certain levels of spinal injury except for short periods.[28] Some papers have emphasized the problems of complications other than the usual ones of the urinary tract and skin, including ruptured diaphragm[29] and calcific deposits.[30] The vocational rehabilitation of many completely paraplegic patients is most encouraging both in the Veterans Administration and in civilian life.[26]

Amputees

There appear to have been considerable gains for these patients, both those with upper-extremity and those with lower-extremity amputations, including hindquarter amputations. Concentrated research has been done with the team approach utilizing engineers and prosthetists working with the medical profession. Research and education have resulted in development of greatly improved upper-extremity prostheses, which have been made available to rehabilitation centers. The education of the limb manufacturers and the professional team, including physiatrists and surgeons, therapists (both physical and occupational) and social workers, has enabled them to utilize these advances. This progress has been summarized in the *Journal* by Thorndike.[31]

Improvements have also been recorded in lower-extremity prosthesis, particularly in the use of the suction socket and the adaptation of this type of muscle contour fitting to all above-knee lower-extremity prostheses. Taylor and Rogers[32] have pointed out the possibility of successful wearing of prostheses for those suffering hindquarter amputations for neoplastic disease. This field of rehabilitation has been most rewarding for those working in it, but improvements in fitting and mechanical action of the prosthesis still remain to be developed. It should be pointed out that there is a need for greater education of the surgeons who are primarily responsible for the aftercare of the amputee patient. They should direct their patients to facilities where properly trained personnel are available to prescribe the newer prostheses and to help the patient learn how to make the best use of the artificial limbs now available.

Poliomyelitis

The recent medical literature on this subject has, of course, dealt largely with the development and utilization of vaccines for the prevention of disease. In spite of all these advances permanently paralyzed patients, who must be watched for the development of deformities during the growing period, remain. One of the greatest deformities is that of scoliosis, and attention is called to articles describing the various types and methods helpful in prevention and treatment.[33,34] Centers dealing with the permanently and severely handicapped have been successful in developing on their own most ingenious adaptive equipment, particularly for quadriplegic patients.[12]

Exercise technics have in general been used as in the past, and no new studies have as yet been critically analyzed to determine the value of the newer proprioceptive facilitation technics. Unreported experiences indicate their value, however. Attention is also called to the utilization of glossopharyngeal breathing for the patients in respirators as a distinct advance in the handling of the chronic residual respiratory embarrassment due to poliomyelitis.[35]

Trauma

The utilization of physical medicine to help rehabilitate the injured is of recognized value, and the subject is so important that it warrants an entire monograph. Unfortunately, this is not at the moment available, and no attempt is made to review the subject here.

Although there is a trend for insurance companies to develop rehabilitation programs separate from hospitals and medical schools[36] it is my opinion that the best future for rehabilitation lies in development of programs within the environment of the general hospital and medical school.[37]

Psychiatric Factors

Those who have dealt with the problems of rehabilitation of the severely ill psychiatric patient are familiar with the utilization of physical medicine and rehabilitation technics, particularly in Veterans Administration hospitals. Patients, families and professional staff have all been impressed by the value of these methods when applied under proper medical direction in such hospitals as well as in civilian institutions where they are available.

It is pointed out, however, that the emotional factors in a nonpsychotic patient are of great importance to rehabilitation when motivation is high among the needs for successful completion of the goal.[38]

Summary and Conclusions

New advances in physical medicine and rehabilitation include further investigations of the biophysical basis of physical treatment. Studies have revealed the relative efficiency of infrared radiation, diathermy and ultrasonic energy.

New information is available on electrodiagnostic technics, particularly electromyography.

More effective methods of neuromuscular re-education have been developed.

In clinical practice the team approach, including physician, therapist, social worker, vocational counsellor and selected consultants, has been emphasized.

The physiatrist by his training has the proper background and interest for leadership in rehabilitation teamwork.

Education of medical students, general practitioners and specialists is needed for future development, combined with research into the fundamental principles of rehabilitation.

In my experience lay interest in medical rehabilitation is greater than that of the medical profession in general owing to so little teaching of the subject in most medical schools.

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MEDICAL INTELLIGENCE

DESCRIPTION OF CHYLURIA

Report of a Case

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CHYLURIA (chyle in the urine) occurs so infrequently that an adequate description is not readily obtained in a standard textbook. Aside from a recent article by Johnston,[1] reports in the literature have indeed been relatively rare.

Surprisingly enough the entity has been known for over three hundred years. Two varieties are described: tropical, or parasitic; and nontropical, or nonparasitic. Tropical chyluria is caused by *Filaria sanguinis-hominis (Wuchereria bancrofti).* They were first found by Demarquay in 1863. Wucherer, in 1866, noted their presence in chylous urine, and Bancroft, in 1877, recovered the adult female worm from a lymphatic abscess. The absence of filaria from the blood or urine does not necessarily exclude the possibility that the patient was not originally a victim of this infection.[2] Yamauchi,[3] in 45 personal cases, was never able to recover the microfilariae from the urine or blood or, in some cases, from the tissues. Again, in 28 cases, Row[4] reports similar negative results. Rarely, as in the case reported by Wucherer in 1866, active filariasis may be present. This unusual feature, together with the presence of classic symptoms seen in chyluria, makes the following case of interest.

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Case Report

Mrs. J. G., a 35-year-old Puerto Rican gravida 4, para 4, was first seen as an outpatient with a chief complaint of passage of urine "looking like milk" and pain in both sides of the back, particularly on the right.

The family history revealed that her mother had had pulmonary tuberculosis in 1952, for which she was treated adequately in a sanatorium in Norwich, Connecticut.

The patient was born in Puerto Rico and attended school to the 7th grade. She worked in the home and later as a government investigator for 2½ years. She came to the United States in November, 1945, residing first in Brooklyn, New York, for 3 months and then making her home in Bridgeport, Connecticut. Inquiry about social habits was noncontributory. Four sons were living and well. She had divorced her first husband in 1954 and remarried in 1955.

The present illness had begun 3½ years before admission (3 months after the birth of her 3d baby). The 1st symptom was pain in both lumbar areas, particularly on the right. It became associated with nocturia (3 times) and diurnal frequency (5 or 6 times). One month later, the patient noted the passage of a milky urine, which persisted throughout the day. She experienced burning on urination, and the act itself became difficult as though something were "stopped up." Frequently, she "passed a lump" and then whitish urine, which remained persistently white throughout the day and night. There was no gross hematuria. She did not seek medical attention until 19 months later. During the 1st year of her illness, she had lost 10.4 kg. (23 pounds) in weight.

Physical examination revealed a markedly undernourished asthenic woman who appeared chronically ill. Tissue turgor was poor, indicating considerable loss of subcutaneous fat. Hair distribution was normal. The conjunctivas were moderately pale, and the fundi appeared to be normal. She had a wizened facial expression. No enlarged lymph nodes were palpable. The heart and lungs were within normal limits. The liver and spleen could not be palpated. Moderate tenderness was elicited over both costovertebral areas, slightly more on the right. The rest of the examination failed to reveal any positive findings.

A fresh specimen of urine was milky, with a specific gravity of 1.017. On standing, a coagulum formed. Analysis demonstrated a ++ test for albumin and a negative test for sugar. Microscopical examination of the sediment showed 2 or 3 white cells per high-power field.

The patient was hospitalized for a complete work-up. Examination of the blood revealed a red-cell count of 3,670,000, with a hemoglobin of 13 gm. per 100 ml., and a white-cell count of 17,500, with 57 per cent segmented neutrophils, 27 per cent lymphocytes, 7 per cent monocytes and 9 per cent eosinophils. The fasting blood sugar was 72 mg., and the blood urea nitrogen 12 mg. per 100 ml. The sedimentation rate was 41 mm. per hour; the total protein was 6.3 gm. per 100 ml., with 4.7 gm. of albumin and 1.6 gm. of globulin. The report of the Venereal Disease Research Laboratory was negative, as was a tuberculin skin test using 1st-strength P. P. D. An x-ray film of the chest was normal. Two specimens of urine were negative for tubercle bacilli on culture and guinea-pig inoculation.

Cystoscopy* revealed a slightly injected and edematous urinary-bladder mucosa. No tubercles were noted. The ureteral orifices were normal in position and appearance. Catheters were passed up each side without difficulty. Retrograde pyelograms showed normal calyxes. The right kidney was in a slightly low position, but in the upright position there was no ptosis. One week after admission filariae were demonstrated in the urine.

For the 1st 3 weeks after cystoscopy and retrograde pyelography the urine became crystal clear throughout the day. The patient felt stronger and gained 0.9 to 1.3 kg. (2 or 3 pounds) in weight. Treatment consisted primarily of diethylcarbamazine† in an effort to eliminate the active phase of the disease. Repeat examinations of blood and urine for filariae were negative. However, 3 weeks after discharge from the hospital, the chyluria recurred, the urine being clear in the morning only. Despite several irrigations of the renal pelvis on each side with 0.5 per cent silver nitrate (1 per cent solution provoked vomiting and undue discomfort) the chyluria persisted. Subsequently, the patient became pregnant. For the last 3 months of her pregnancy, the urine became completely clear. Hydramnios necessitated induction of labor, and a normal male baby was delivered. Nine days later, chyluria was again noted, persisting throughout the day and night. The patient has refused any further therapy.

*Done by Sidney Beck, M. D.

†Available as Hetrazan from Lederle Laboratories, Pearl River, New York.

Discussion

The most widely accepted explanation for the etiology of chyluria is the one first proposed by Carter[5] in 1862 and by Ackermann[6] in 1863. Briefly, the theory postulates a mechanical obstruction in the lymphatics between the intestines and the thoracic duct provoking stasis, lymph varices and insufficiency of the valvular system of the lymphatics. A varix may rupture and cause a lymphaticourinary fistula with chyle flowing into renal pelvis, ureter or bladder. The renal lymphatics are the most easily ruptured of the entire lymphatic system. Apart from filariasis, other conditions such as tumors, inflammatory disturbances or even a pregnant uterus may lead to lymph stasis. Several authors[2,7,8] have stressed the importance of pyelolymphatic backflow, indicating the presence of a direct communication between the lymphatics and the urinary tract at the fornix or the fornices of minor calyxes. Associated renal infection is usually a precipitating factor. Yamauchi[9] considers pyelonephritis in varying degrees to be present in practically all cases of chyluria.

Symptoms usually start in early and middle life but may occur in all age groups. An awareness of the condition is most important in diagnosis. The most striking symptom is the passage of milky urine, usually sudden in onset and frequently the only presenting symptom. The chyluria may be intermittent or continuous. The urine may become a gelatinous mass on standing. Usually, the patient has dysuria and discomfort in the lumbar area and complains of passing clots. If there is an associated hematuria, the urine may be pink tinged. The loss of subcutaneous fat results in a characteristic wizened facial expression.

The major surprise develops when the urine is examined microscopically. Expecting this to be a severe case of pyuria, the physician or technician will be nonplussed to find few white cells in the sediment unless the complicating pyelonephritis is severe. High-speed centrifuge will not yield any separation of the fat. The solution is remarkably stable, containing 2 to 4 per cent fat. A specimen from the patient described above was left standing for three months with surprisingly little change. The fat is in molecular form in a state of colloidal suspension. Carter,[5] in a right-kidney specimen, found it to be fractionally 35 per cent urine and 65 per cent chyle. The albumin content may vary from 3 to 3.5 per cent. Lecithin, cholesterin, fibrinogen and soaps are also present in the urine. To confirm the presence of chyle in the urine, Sudan III in butter given orally will appear in the urine. Ether will extract the dye and the chyle. Occasionally,[2,8] pyelolymphatic backflow may be demonstrated by retrograde pyelography.

The main conditions to be ruled out in a differential diagnosis are lipuria, marked pyuria and pseu-

dochylous urine. Lipuria, which shows an absence of fibrin and the presence of fat in droplet form, is seen with fractures, eclampsia, diabetes, degenerative renal disease and intoxication due to phosphorus, arsenic and carbon monoxide. Microscopical examination will easily differentiate pyuria. Finally, pseudochylous urine differs from true chyluria in that the specific gravity of the former is less than 1.012 whereas that of the latter is greater than 1.012. The total solid content of true chyle is about 4 per cent, and that of pseudochyle less than 2 per cent. Total fat content of true chyle is 0.4 to 4 per cent whereas that of pseudochyle is lower.

The active infection may be treated with diethylcarbamazine[9] at a dosage of 2 mg. per kilogram of body weight given three times a day for seven days. The regimen of therapy for the chyluria consists of a low-fat diet and irrigation of the renal pelvis on the affected side with a sclerosing solution, preferably 1 or 2 per cent silver nitrate.[4] Prognosis concerning life is good, but relapses frequently occur.

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BY THE LONDON POST

Postgraduate Medicine in London — The Art of Self-Criticism — Working Mothers

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LONDON, ENGLAND

THE Postgraduate Medical School of London received its Royal Charter twenty-five years ago. Ten years previously the first Minister of Health, Dr. Christopher Addison, had appointed a committee to investigate the needs of medical graduates for further education in London. It was upon the recommendation of this committee that the Postgraduate Medical School was established at Hammersmith Hospital. Although early development was hampered by the financial crisis of 1931 and further expansion was delayed by World War II the achievements of the school in the twenty-five years of its existence have been considerable.

When opening the school in 1935, King George V said he hoped it would play an imperial role in the winning and dissemination of medical knowledge in the relief of suffering among people at home and overseas and that it would enable doctors of all lands to come together in a task in which all must be allies and helpers.

Since that time 12,000 medical graduates from 72 different countries have attended the school. The majority have come from Britain and the Commonwealth, but more than 750 have come from the United States, 723 from Europe and 941 from other parts of the world.

The policy of the school has always been to educate rather than to teach. Because of this the formal course has never been a characteristic feature of the school. Rather, it has been the aim to provide opportunities for research and for free discussion of current problems so that the students may educate themselves and receive a balanced training in the practice of clinical medicine. Indeed, many of the students have collaborated with the permanent staff in important research projects on these lines.

To increase the scope of postgraduate medical education now offered in London, the University in 1945 established the British Postgraduate Medical Federation. This incorporates the Postgraduate Medical School with a number of institutes in the leading specialist hospitals in London. Thus, the Brompton Hospital provides facilities for postgraduates to study diseases of the chest; the National Hospital for Nervous Diseases provides facilities in neurology, and Great Ormond Street covers the field of pediatrics.

The rapidly increasing activities of the Postgraduate Medical School have now made it necessary for it to extend its accommodation. The school, unlike the much older undergraduate teaching schools, has unfortunately neither endowments nor subscribers. The annual university grant provides only for running expenses, and cannot provide for capital works. It has therefore become necessary to make a public appeal for support, and it is a happy coincidence that the appeal for £750,000 is being launched under the patronage of the Earl of Athlone, who was the chairman of the committee that originally, in 1921, recommended the school's foundation. It is to be hoped that a satisfactory response will be forthcoming so that the Postgraduate Medical School may maintain its position as one of the leading postgraduate medical centers in Europe.

* * *

The Croonian Lectures of the Royal College of Physicians of London were delivered this year by Dr. Arthur Douthwaite, senior physician to Guy's Hospital. Stimulated no doubt by William Croone's own critical mind, which was ever searching for truth, Dr. Douthwaite dealt in these lectures with a series of diagnostic mistakes that he had recorded over twenty-five years.

Dr. Douthwaite pointed out that the layman finds it difficult to understand how the specialist or consultant can make a mistake and is only too ready to take him to law if he does so. Yet, he said, mistakes are inherent in the pursuit of a progressive science, and one must not be too disturbed by them so long as mental discipline and self-respect are preserved intact. At the same time one must learn to profit from mistakes; it was Oscar Wilde who said that experience is the name everyone gives to his mistakes.

Dr. Douthwaite said that there are a multitude of impediments upon the road to correct diagnosis. Some causes of failure lie with the physician or the surgeon; others stem from the patient or the obscurity of his disease. The patient's mental ability, his attitude, his fear of disease and his inability to express himself clearly are all important factors, and at the same time there are always the unpredictable vagaries of diseases.

In approaching the patient Dr. Douthwaite stresses the importance of history taking and simple clinical examination and urges physicians always to look at the x-ray films themselves and to interpret the mass of other special investigations in the light of the clinical findings. Accurate, specific diagnosis should be the aim of the clinician, and such modern parrot cries as adaptations, reactions, collagen diseases, cerebral catastrophe and cardiac episodes are to be deplored. Similarly, one must beware of bias and overswing in favor of current theories. Sometimes, the rise in the number of diagnoses has been justified by a true increase in disease, but there is always the danger that prejudice and mental laziness will lead to a currently favored diagnosis on insufficient grounds.

Mistakes made because of the vagaries of disease can usually be traced to unusual symptoms rather than to puzzling physical signs. Dr. Douthwaite said that there are probably few patients whose history may not reveal unreasonable obsessions, fears and anxieties in the course of their lives and that perhaps all men are potential neurotics. Nevertheless, the patient above all others of whom one must constantly beware is the neurotic with organic disease. There must be few physicians who have not been trapped by the neurotic who has "cried wolf" just once too often.

In his closing remarks, Dr. Douthwaite said that self-criticism is far more important than criticism of others, and, quoting Matthew Arnold, he concluded that criticism is a disinterested endeavor to learn and propagate the best that is known and thought in the world.

* * *

The mother who goes out to work seems to have become a permanent feature of contemporary society. Originally going out to work for economic reasons and encouraged to do so by the shortage of labor, many married women with children have found that they are able to combine their household duties with part-time employment outside their homes, and they are doing so in ever-increasing numbers.

More women are marrying, many very young, and in general their families are small. When her youngest child ceases to claim her full attention, the young mother can look forward to many active years ahead. These facts, together with the persistence of a high cost of living and a state of full employment, are the main reasons for the increasing numbers of working mothers.

Die-hards who insist that the mother's place is in the home are shocked by this situation. The experts in child guidance are convinced that the modern lack of discipline and the high prevalence of juvenile delinquency are associated with unstable home conditions and believe that these are often due to the mother's absence from the home. On the other hand many mothers claim that they have been tied to the kitchen sink too long; their escape from the confines of their homes makes them better tempered on their return, and they claim that the result is a more harmonious atmosphere when they are at home, with benefit to husband and children alike. The reactions of the husbands vary, but no doubt they can fend for themselves. It is the effect on the children that is really more important — what this really is, time alone will tell.

CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 42521

PRESENTATION OF CASE

A sixty-five-year-old salesman entered the hospital because of pain in the chest.

Two years previously there was an episode of substernal discomfort that lasted for one hour. Three or four similar, shorter episodes that were related to exertion occurred during the next two years. Two hours before entry the patient noted a severe, nonradiating "uncomfortable feeling" in the middle of the chest that was similar to the previous discomfort, was accompanied by sweating and weakness and was not relieved by nitroglycerin. There was no orthopnea, paroxysmal nocturnal dyspnea or edema of the ankles. There was no history of rheumatic fever.

Physical examination showed an obese, pale man lying quietly in bed. There was no distention of the veins in the neck. Examination of the chest revealed bilateral basal rales. The left border of cardiac dullness extended 2 cm. beyond the mid-clavicular line. The cardiac sounds were poor, and there was a bigeminal rhythm. One observer felt the edge of the liver 4 cm. below the right costal margin. The upper border of liver dullness was in the sixth intercostal space. There was no peripheral edema. Neurologic examination was negative.

The temperature was 98°F., the pulse 118, and the respirations 20. The blood pressure was 130 systolic, 80 diastolic.

The urine gave a + test for albumin. Examination of the blood revealed a hemoglobin of 16.5 gm. per 100 ml. and a white-cell count of 22,200, with 87 per cent neutrophils. The nonprotein nitrogen was 27 mg., and the cholesterol 263 mg. per 100 ml. The sodium, potassium, chloride and carbon dioxide were normal. The prothrombin content was 55 per cent.

During the first hospital day there were repeated episodes of ventricular tachycardia, each lasting up to three minutes. These were controlled with Pronestyl given intravenously. Quinidine and digitoxin were begun. The blood pressure gradually rose to 190 systolic, 120 diastolic, six hours after admission. Thereafter, it gradually fell to normal. An electrocardiogram on the first hospital day showed a normal sinus rhythm at a rate of 85; the PR and QRS intervals were 0.20 and 0.08 second, respectively; the ST segments were depressed in Leads 2, 3 and aVF and markedly elevated in Leads V_1 through V_5; the R waves were absent, and the T waves were tall and peaked in Leads V_1 through V_4. Because of a rise in the temperature to 101.2°F. and persistent moist rales at the right-lung base, penicillin and streptomycin therapy was begun on the first hospital day. The temperature gradually fell to normal, and the pulmonary rales cleared. With anticoagulant therapy the prothrombin content ranged from less than 10 per cent to 37 per cent. An electrocardiogram on the second hospital day showed a normal sinus rhythm at a rate of 95; the PR and QRS intervals were 0.16 and 0.08 seconds, respectively; the T waves were diphasic in Leads 1, 2, aVF and V_6; the R waves were absent and the ST segments were elevated in Leads V_1 through V_4; the T waves were inverted in Leads V_2 through V_4. Three days later an electrocardiogram showed a normal rhythm with an infrequent atrial premature beat at a rate of 75; the T waves were low with slightly sagging ST segments in the limb leads; the R waves were absent, and there was moderate elevation of the ST segments in Leads V_1 through V_5. Convalescence continued, with gradual ambulation during the fourth week after admission. The heart sounds were normal. Examination of the abdomen was negative. There was no venous distention or peripheral edema. An electrocardiogram on the twenty-third hospital day showed a normal sinus rhythm at a rate of 85; the PR and QRS intervals were 0.17 and 0.07 seconds, respectively; the axis was normal; the T waves were inverted in Leads 1 and aVL; there were low to absent R waves in Leads V_1 through V_5 and slight elevation of the ST segments and diphasic T waves in Leads V_2 through V_4. Two days later the patient noted a nonradiating, nonpleuritic pain in the left flank and lower portion of the left side of the chest that occurred while he was on a bedpan. There was no pain in the calves. The white-cell count was normal. Subsequently, there was momentary pain but no tenderness in both costovertebral angles caused by walking or prolonged sitting. An x-ray film of the chest was normal. An intravenous pyelogram was normal except for a filling defect in the floor of the urinary bladder. Films of the lumbar spine demonstrated degenerative changes in the region of the apophyseal joints. The urine was normal. The serum nonprotein nitrogen was 28 mg., the uric acid 6.1 mg., the calcium 9.2 mg., and the phosphorus 2.7 mg. per 100 ml. The alkaline phosphatase was 19.4 units.

On the forty-first hospital day jaundice was noted. There was no abdominal tenderness. The liver and

spleen were not palpable. Examination of the blood revealed a hemoglobin of 13.8 gm. per 100 ml. and a white-cell count of 8400. The bilirubin was 6.2 mg., the total protein 7.3 gm., the albumin 3.9 gm., the globulin 3.4 gm., the fasting blood sugar 111 mg., and the blood ammonia 52 microgm. per 100 ml. The alkaline phosphatase was 26.5 units, the prothrombin content 14 per cent, the thymol turbidity 2.5 units, with a negative flocculation, the cephalin flocculation +++, the Coombs test negative, and the urinary urobilinogen 1.3 and 3.1 Ehrlich units. A stool specimen was brown and gave a negative guaiac test. An electrocardiogram showed only minor changes since the previous tracing. X-ray films of the chest were normal except for an increase in the transverse diameter of the heart. An upper gastrointestinal series demonstrated a nodularity along the medial aspect of the gastric fundus near the cardia (Fig. 1 and 2). Films of the thoracic spine demonstrated a compression fracture and increased radiolucency of the ninth thoracic vertebra. A film of the skull was normal.

FIGURE 1. *Right Anterior Oblique View of the Stomach. The fundus is irregular and somewhat nodular in outline, particularly medially.*

Subsequently, the patient became confused, with increasing jaundice. On the fifty-second hospital day he was somnolent. The abdomen was slightly distended. He passed a chalky stool. The direct serum bilirubin was 10.6 mg. and the total 14.4 mg. per 100 ml., the cholinesterase 0.25 delta pH unit per hour, and the blood ammonia 72 microgm. per 100 ml. One observer noted a slightly tender epigastric mass. There was a recurrence of the pain in the back with tenderness to deep pressure in the region of the ninth thoracic vertebra and in the posterior axillary line in the region of the tenth rib on the right. The mental confusion gradually progressed to coma. Rapidly developing ascites was noted beginning on the fifty-seventh hospital day. Five days later the serum bilirubin was 21.8 mg. per 100 ml., and the amylase 2 Russell units. In spite of daily doses of vitamin K the prothrombin content was 16 per cent. On the sixty-fifth hospital day the patient vomited about 400 ml. of black blood. An additional 100 ml. was aspirated from the stomach. Petechial hemorrhages over pressure-sustaining areas and more pronounced bleeding into the skin at the sites of venipunctures were noted. He died on the next day.

FIGURE 2. *Lateral View of the Stomach. The body is pressed upon anteriorly by the enlarged liver.*

DIFFERENTIAL DIAGNOSIS

DR. BRIANT L. DECKER*: May I see the x-ray films?

DR. JOSEPH HANELIN: A representative film of the chest taken early in the hospital course shows no significant change in the lungs; the heart is slightly enlarged along the left ventricle. There is a defect at the base of the bladder, which could be caused by some prostatic enlargement, among other things. One finding of interest is a somewhat nodular contour to the gastric fundus, more marked medially; in a lateral projection there appears to be an excessive amount of pressure upon the anterior surface of the stomach, such as might be produced by hepatic enlargement. The nature of the gastric abnormality is not too clear from the films, nor was it at fluoroscopy; it might conceivably result from an intrinsic gastric carcinoma, but more probably from extrinsic pressure, perhaps on the basis of involvement of the pancreas or lymph nodes in the area. Another finding is compression of the ninth thoracic vertebra, which shows increased radiolucency, so that there is probably a neoplastic lesion of this vertebral segment. The remainder of the skeleton is normal.

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DR. DECKER: Do you see any evidence of abnormality of the thoracic vertebras at the time of admission?

DR. HANELIN: At the time of admission there is a suggestion of involvement of one of the lower thoracic bodies. I can't be positive about it in the early examination.

DR. DECKER: Is it comparable to that one?

DR. HANELIN: I think in the interval, which is almost a month, further compression of the involved body has taken place.

DR. DECKER: Are the lungs clear? You do not see any evidence of metastatic disease?

DR. HANELIN: Nothing very obvious, although some accentuation of markings may denote early lymphatic spread.

DR. DECKER: Do you think that the nodularity here (lesser curvature of the cardia) might be caused by the pressure of a large, carcinomatous pancreas?

DR. HANELIN: Yes.

DR. DECKER: That is not too far away?

DR. HANELIN: No; the tail of the pancreas frequently impinges upon that portion of the stomach.

DR. DECKER: Do you see, in any other film, evidence of hepatic enlargement?

DR. HANELIN: No; I do not, but it is suggested by the lateral film of the stomach.

DR. DECKER: Are there varices?

DR. HANELIN: One wonders whether there might be small varices; there are certainly not large varices.

DR. DECKER: What is that?

DR. HANELIN: That is the left paravertebral pleural reflection demarcating the paraspinal soft tissues, which may be slightly widened, possibly by neoplasm.

DR. DECKER: Can you see that in any other films?

DR. HANELIN: Not too well.

DR. DECKER: I think that there is no question that the patient had a severe myocardial infarction. He had had symptoms of angina pectoris for two years; he entered the hospital with characteristic pain of two hours' duration, unrelieved by nitroglycerin and accompanied by sweating and weakness. Physical examination revealed an elevated temperature and pulse, pallor and basal rales. The heart was enlarged, with poor sounds, and arrhythmia developed. The blood pressure was apparently found to be lower than it had been in the past, for it rose to moderately high levels with treatment. Laboratory tests showed consistent findings, including a white-cell count of 22,000, with 82 per cent neutrophils (I am surprised that the transaminase was not determined). Serial electrocardiograms indicated a large, anterior infarct and showed a characteristic evolution throughout the stay in the hospital. He was given anticoagulants, and in spite of initial evidence of congestive heart failure and arrhythmia, he seemed to be getting along well until the twenty-fifth hospital day. At that time he had pain, which I believe was probably produced by the compression fracture of the ninth dorsal vertebra. There was a question whether there was a pulmonary infarction. Appropriate studies were done, but the only abnormal finding was the elevated alkaline phosphatase of 19.4 units, which gave the first evidence of liver disease, except that on admission to the hospital one physician remarked that the liver was 4 cm. below the right costal margin. The prothrombin time of 55 per cent may have been on the basis of the congestive heart failure. We do not know the dosage of anticoagulants required to keep the prothrombin time at the level at which it was kept. That might have given us a clue to liver difficulty.

There was no information about the course from the twenty-fifth to the forty-first hospital day, but I assume that the patient was not well because he was not discharged. On the forty-first day jaundice was first noted, and tests of liver function gave evidence mainly of obstructive jaundice. The serum bilirubin was elevated; the alkaline phosphatase rose to 26.5 units, and the prothrombin content was 14 per cent. (I assume that he was no longer receiving anticoagulants.) The slight elevation of the serum globulin and slight decrease in the serum albumin could also indicate cellular disease. The equivocal or slightly abnormal cephalin flocculation could well have resulted from the slightly elevated serum globulin. The results of these tests ruled out acute parenchymatous liver disease. There was no hemolytic disease, as shown by the negative Coombs test, the lack of anemia and the slight elevation of the urinary urobilinogen.

At this time the x-ray examination, including that of the dorsal spine, demonstrated what I believe was the underlying disease. Thereafter, the course was rapidly downhill, with increasing jaundice, confusion and coma. There was evidence of further damage of the liver cells, as indicated by the low cholinesterase, the slight elevation of blood ammonia level and the failure of the prothrombin time to respond to vitamin K injection. Jaundice continued to increase; ascites developed rapidly, and in the few days before death hemorrhagic manifestations appeared.

It seems to me that this patient had carcinoma, involving the ninth thoracic vertebra and the liver. The carcinoma in the vertebra is indicated by the x-ray findings of collapse and translucency; carcinoma in the liver is suggested by the early finding of an elevated alkaline phosphatase and the very rapid progression of the hepatic failure.

What was the source of this carcinoma? If a diagnosis of carcinoma involving the liver is made, I believe one always has to assume that it is metastatic until proved otherwise and look for help in the x-ray films and the symptoms. The gastrointestinal series was somewhat suggestive of carcinoma of the cardia of the stomach, but no symptoms of that were reported in the protocol. Furthermore, the stools were guaiac negative. The patient had no anemia. There was some evidence in the gastrointestinal series of widening of the duodenal loop. Dr. Hanelin, is that true?

DR. HANELIN: The loop is broad, but I cannot be

sure that the widening is produced by tumor. The patient was of sthenic build, and a wide loop is often seen in such patients.

DR. DECKER: There is a possibility that the loop is widened. The nodularity of the medial aspect of the cardia, as Dr. Hanelin has stated, could be caused by an enlarged pancreas or enlarged lymph nodes. Also, one of the observers, toward the end of the patient's life, noted a tender epigastric mass, which may have been the pancreas. There was no history of the characteristic pain in the back that accompanies carcinoma of the pancreas. That is why I wondered whether the pain that occurred on the twenty-fifth day was caused by a lesion in the pancreas, although its exacerbation with the patient sitting and walking certainly suggests a vertebral lesion. No microscopical studies of the stools were done to try to determine pancreatic function. The serum amylase was normal. There was nothing to suggest cancer of the colon, prostate or bladder.

To assume that the patient had a primary carcinoma of the liver, a hepatoma, I should have evidence of cirrhosis, which is present in a very high percentage of cases of hepatoma. I do not have that evidence. There was no history of alcoholism, and the physical examination did not suggest cirrhosis. There was no enlargement of the spleen and no spider angiomas. About the only indication of cirrhosis was the slight change in the serum proteins. Moreover, there was no indication of a large mass under the diaphragm, which is what frequently occurs in hepatoma. The same arguments apply to cholangioma. It is rarer than hepatoma. Cirrhosis is present in about half the cases, and extrahepatic metastases are unusual. Furthermore, I should expect the liver to be very much enlarged.

I believe that the most likely diagnosis is carcinoma of the body or tail of the pancreas, with direct extension into the regional lymph nodes and the paravertebral space and with involvement of the ninth thoracic vertebra. I also believe that the portal vein was involved, with the rapid development of the ascites as a result. The hemorrhagic manifestations were probably produced by liver failure.

DR. JOSEPH W. GARDELLA: Our reasoning in this case was similar to Dr. Decker's. We thought at first that the patient had hepatocellular disease, but wondered whether the rise in the alkaline phosphatase might not have been caused by metastatic bone disease and, therefore, also considered hepatic disease of malignant type. This became more and more likely as the disease progressed. A paracentesis was performed, and upon cytologic study of the fluid, the diagnosis was made clear.

DR. ALLAN L. FRIEDLICH: One thing that was not brought out in the protocol was the peculiar somnolence and the lethargy of the patient after admission to the hospital; the cause of that was not clear at that time.

DR. GARDELLA: It never was clear. Soon after the myocardial infarct and long before clinical jaundice he exhibited a marked change in personality and became very intractable, rather confused and almost comatose. We wondered about Dr. Friedlich's suggestion that he might have had Pronestyl intoxication, but could find no evidence in the literature that cerebral damage results from Pronestyl.

DR. FRIEDLICH: He had received Pronestyl intravenously in large amounts continuously for about three days.

CLINICAL DIAGNOSES

Metastatic carcinoma of liver, ? from ampulla of Vater, ? from stomach.
Old anteroseptal myocardial infarction.

DR. BRIANT L. DECKER'S DIAGNOSES

Carcinoma of body or tail of pancreas, with direct extension to regional lymph nodes, liver, vertebra and portal vein.
Myocardial infarction.

ANATOMICAL DIAGNOSES

Adenocarcinoma of body and tail of pancreas, with metastases to liver, pleura, pericardium, lymph nodes, adrenal gland, appendix, lungs and bone.
Coronary-artery disease, with myocardial infarction, anterior and apical (nine weeks), coronary sclerosis, severe, and thrombosis, anterior descending branch of left coronary artery.
Ascites.

PATHOLOGICAL DISCUSSION

DR. EDGAR B. TAFT: This patient at autopsy was quite jaundiced. The stomach contained 1500 ml. of bright-red blood, but no bleeding points could be demonstrated by the prosector either in the esophagus or in the stomach. I think this was a manifestation of the generalized bleeding tendency that the patient had.

The heart was markedly enlarged, weighing 550 gm. The coronary arteries were sclerotic, particularly the left, and in the anterior descending branch of the left coronary artery 1.5 cm. from its origin there was an old thrombus, which extended for 2 cm. along the artery. The anterior ventricular wall was soft to palpation over an area 4 by 3 cm., and on section showed thinning and replacement of the musculature with fibrous tissue. Microscopically, there was still active proliferation of fibrous tissue, with continuing removal of a few small, persistent nests of necrotic muscle fibers. The findings were consistent with the nine-week history.

As Dr. Decker predicted, the pancreas was the site of a primary tumor. The tail and distal portion of the body were replaced by a large mass of pink, firm tumor. In other areas there were small, white flecks

of fat necrosis. The splenic vein was thrombosed in the region of the tumor, but this was the only other thrombosis that was found. The portal vein was clear of thrombi. The leg veins were not examined. The liver weighed 2700 gm.; three quarters of it was occupied by tumor. The largest mass of tumor was in the quadrate lobe and extended into the left lobe of the liver. I should not be surprised if this was where the main obstruction to the bile duct was, because with pressure over the gall bladder bile flowed freely from the ampulla of Vater at the time of autopsy. There were also tumor metastases to the pleura, pericardium, lungs, lymph nodes of various sites and the right adrenal gland, to the appendix and to both the eighth and ninth thoracic vertebras, the fifth rib on the right and the seventh rib on the left. We did not see tumor in the neighborhood of the tenth rib, where the patient had the pain, so I suspect that pain was from compression of the involved vertebras. Microscopically, the tumor was in part mucinous, with signet-ring cells, and was characteristic of a well differentiated adenocarcinoma of the pancreas.

CASE 42522

Presentation of Case

A forty-nine-year-old Guatemalan businessman entered the hospital because of abdominal pain.

For six or seven months before admission he had an intermittent, nonradiating, aching pain in the right upper quadrant of the abdomen that was unrelated to meals or time of day and was relieved by drinking of Coca-Cola. At the same time persistent fatigue, a decrease in appetite and intermittent constipation were noted. About three months before admission his physician felt a mass in the right flank. An upper gastrointestinal series was allegedly normal. There was no loss in weight. No melena or change in bowel habits was noted. There was a past history of a moderate alcoholic intake.

Physical examination showed a slightly obese man who did not appear ill. There was no jaundice or lymphadenopathy. The chest was emphysematous. A smooth, firm, apparently cystic mass of the abdomen, measuring 15 cm. by 20 cm., was present in the anterior portion of the right flank. The mass appeared to be attached to the liver and descended with respiration. The edge of the liver, which was smooth, hard and nontender, was felt 8 or 10 cm. below the left costal margin and 12 cm. below the xiphoid process. No other masses were noted. The spleen was not palpable.

The temperature was 99°F., the pulse 90, and the respirations 20. The blood pressure was 140 systolic, 70 diastolic.

The urine was normal. Examination of the blood revealed a hemoglobin of 15.8 gm. per 100 ml. and a white-cell count of 6100, with 60 per cent neutrophils, 29 per cent lymphocytes, 9 per cent monocytes, 1 per cent eosinophils and 1 per cent basophils. The total protein was 8 gm., the albumin 5.5 gm., the globulin 2.5 gm., the nonprotein nitrogen 37 mg., and the fasting blood sugar 92 mg. per 100 ml. The alkaline phosphatase was 3 units. The prothrombin content was 100 per cent, the cephalin flocculation +, and the bromsulfalein retention 5 per cent. The serum electrophoretic pattern showed an increase in the gamma globulin. A stool specimen was greenish brown and gave a negative guaiac test. X-ray films

Figure 1. *Intravenous Pyelogram.*
The large mass in the right side of the abdomen extends from the level of the diaphragm to below the iliac crest and causes downward and medial displacement of the right kidney (arrows).

of the chest demonstrated emphysema. An intravenous pyelogram showed the right kidney to be displaced downward and medially by a mass in the right upper quadrant that was indistinguishable from the liver shadow (Fig. 1); the lower edge of the mass overlay the superior aspect of the ilium; no calcification was seen in the mass; there was no hydronephrosis; the left kidney was normal; trabeculation of the urinary bladder was noted. A barium-enema examination revealed that the tumor pressed upon the proximal portion of the transverse colon. A cholecystogram demonstrated normal function of the gall bladder, which appeared to be displaced upward by the abdominal mass.

An operation was performed on the sixth hospital day.

Differential Diagnosis

Dr. William C. Quinby, Jr.*: The problem is to determine the origin of the mass, what organs it involved and what the nature of it was. The illness of

*Assistant in surgery, Massachusetts General Hospital.

six or seven months' duration speaks for a chronic process and gives no definitive clue about the organs involved or the nature of the process. Fatigue was noted, but absence of weight loss throws emphasis away from a rapidly progressive malignant tumor. On physical examination the patient looked well, and the mass was described as cystic. The mass was large and was in the anterior portion of the right flank. Its attachment to the liver must have been a strong clinical impression. The liver edge at the epigastrium in the left upper quadrant was definitely below the normal level. If the upper edge was in the normal position, I cannot escape the implication of a markedly enlarged liver. The data from the clinical laboratory do not help us very much. I think a hemoglobin of 15.8 gm. per 100 ml. in a man with emphysema is all right. We have no lead from the white-cell count. The total protein of 8 gm. per 100 ml. is somewhat high, but, I think, still normal; the albumin-globulin ratio is also normal. The increase in gamma globulin noted in the electrophoretic pattern is probably not helpful since many chronic inflammatory processes in the liver or body may produce an increase in the gamma globulin. The specific tests of hepatocellular function were normal. Therefore, the effects of the mass on the patient do not appear to have been dramatic. Dr. Hanelin, can you help localize the mass?

DR. JOSEPH HANELIN: The films of the chest show a marked amount of pulmonary emphysema, which may be a factor in making the liver palpable, as a result of depression of the diaphragm. The right leaf of the diaphragm is slightly elevated, but not much more than normally. There is a large, homogeneous shadow in the right side of the abdomen that cannot be distinguished from the liver, the lower edge of which overshadows the upper portion of the iliac wing. It contains no calcification. In the intravenous pyelogram the right kidney is displaced downward and medially. The mass also presses upon the hepatic flexure and proximal transverse colon; one can see in the oblique film that it imprints these structures along their anterior surfaces. Apparently, the lesion also affects the position of the gall bladder, which lies distinctly higher and somewhat more medial than usual.

DR. QUINBY: Can you point out the mass in the oblique film?

DR. HANELIN: Only by implication from displacement of adjacent structures; the colon is pushed anteriorly. The lower edge of the mass is roughly opposite the upper portion of the ilium and not well defined.

DR. QUINBY: Is the right ureter affected?

DR. HANELIN: The proximal portion of the right ureter is displaced somewhat toward the mid-line.

DR. QUINBY: Do you think that the right kidney was once at a normal level much higher than that shown?

DR. HANELIN: I think, in the presence of this large mass, one may assume that the kidney is being displaced by it; it lies adjacent to the kidney.

DR. QUINBY: In the oblique films is the kidney displaced anteriorly?

DR. HANELIN: Yes; toward the mid-line and slightly anteriorly.

DR. QUINBY: The reason that I paid so much attention to the position of the right kidney is that in my experience intraperitoneal masses that expand slowly do not displace retroperitoneal structures. I think it is still open to argument whether the right kidney had been at the level of the fifth lumbar vertebra all this patient's life or whether it had been displaced by the mass. I shall have to take Dr. Hanelin's interpretation that in all probability it was displaced by the mass. I must therefore include retroperitoneal structures, as well as intraperitoneal ones, in the discussion.

Not long ago in this hospital we saw a cystic tumor of the adrenal gland that had displaced the left kidney. That tumor was only about the size of a baseball, and the patient showed no effects of increased production of adrenal hormones. It was exceedingly difficult to diagnose, and the displacement of the kidney was important in the diagnosis. I cannot exclude a similar adrenal cyst in this case except on the basis of size, which would be most unusual.

Next, there is a whole realm of retroperitoneal growths, which I shall merely group under the heading of lymphoma. I do not see evidence of extensive disease of the lymph nodes retroperitoneally, nor were there other enlarged lymph nodes. The patient had not been very sick; he was afebrile, and he had not lost weight.

To arrive at a diagnosis I shall take the evidence from the clinical examination and the x-ray films and say that the mass arose in the right lobe of the liver — indeed, that it was part of the liver. What enlargements of the liver might present in this fashion? I believe that I can eliminate primary or secondary malignant tumors on the basis of the size of the mass and the lack of evidence of generalized debility of the patient.

Benign solid tumors of the liver are very rare. Hemangiomas — if one calls them solid tumors — are slightly more common. They occur most frequently in the left lobe and in women more often than in men. They may be of any size, from that of a small raspberry to a large, terrifying, soft tumor in the substance of the liver.

Another process to consider is hepar lobatum, seen in late syphilis. On physical examination there was no evidence of such large nodules in the liver edge, so I shall exclude it.

Cysts of the liver occur either as simple cysts without known cause or secondary to parasitic infection. I do not believe that this patient had echinococcal disease. I believe an echinococcal cyst of this size would con-

tain some calcification and would be more accurately demonstrable. Multiple cysts in the liver have occurred with polycystic kidneys, but are usually much smaller than this. The liver edge palpable in the left upper quadrant and epigastrium makes me suspect that there may have been a generalized involvement. Nevertheless, I shall say that a simple solitary cyst of the liver was the cause of the mass. I am forced to abandon my thesis about the displacement of the kidney and say that my clinical experience may be erroneous or that the patient had always had an ectopic kidney.

It will be interesting to know what sort of operation was done. On the basis of the entire evidence, in all probability this patient was explored for a cystic tumor thought to originate in the right lobe of the liver posteriorly.

A Physician: You have not mentioned the pancreas?

Dr. Quinby: I thought of the pancreas. Although pancreatic cysts or benign pancreatic tumors can appear without any significant previous history, they usually exhibit a more dramatic history of biliary-tract disease than the lesion in this case did. Furthermore, they usually present anteriorly between the stomach and the transverse colon. After acute pancreatitis the necrotic material may gravitate and ultimately present almost anywhere, but this was a mass in the anterior portion of the right flank and there was nothing to incriminate the biliary tree or to suggest attacks of pancreatitis. I suppose that there could have been a congenital cystic derangement of the pancreas, but that is even more rare.

Dr. Daniel S. Ellis: We were all impressed by the patient's apparent well-being; he did not look as though he were ill. It was difficult to obtain details of the history because of language difficulty, but we believed that he had had symptoms for at least a year. Because of the apparent displacement of the kidney, I believed that he had a retroperitoneal tumor, either a cystic tumor or a lymphoma. After we saw the pyelogram, we could not exclude a large cyst involving the right kidney. Both Dr. Claude E. Welch and I sent the patient to the operating room believing that he had a retroperitoneal tumor, the exact nature of which was undetermined. We had considered all the conditions that Dr. Quinby mentioned. The house officer's original note mentioned cyst of the liver, echinococcal cyst, pancreatic cyst and renal tumor. We thought that the mass was not a part of the liver — at least not of the anterior surface of the liver — because we could palpate between the costal margin and the tumor mass.

Clinical Diagnosis

Retroperitoneal tumor.

Dr. William C. Quinby, Jr's, Diagnosis

Solitary simple cyst of liver.

Anatomical Diagnosis

Echinococcal cyst of diaphragm, with extension to liver.

Pathological Discussion

Dr. George S. Richardson: I saw the operation, which was performed by Dr. Claude E. Welch. The mass was a large echinococcal cyst. It had only a limited attachment to the right lobe of the liver but had quite a wide attachment to the inferior surface of the right leaf of the diaphragm. Because of this attachment it was impossible for Dr. Welch to remove the cyst without entering it. Thus, an initial attempt to reach the tumor through a thoracoabdominal incision would have involved sacrificing the right leaf of the diaphragm and would have resulted in contamination of both the abdominal and the pleural cavities with the contents of the cyst. The huge cyst appeared to arise almost completely from the diaphragm, rather than from the liver, as one would ordinarily expect. Was that your impression, Dr. Ellis?

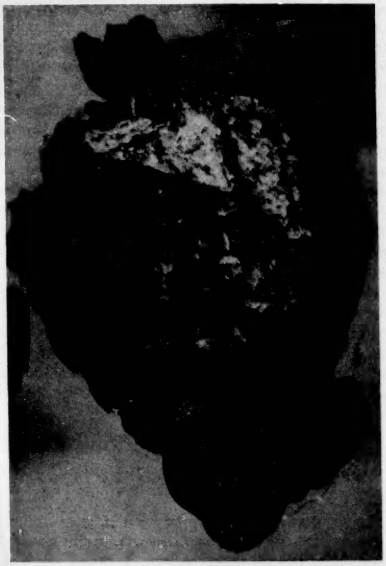

Figure 2.

Dr. Ellis: The point of origin was not clear at the time the abdomen was opened. At first it appeared that the cyst arose from the kidney; after it was freed from the kidney it seemed that the liver was the point of origin. Then it could be freed almost completely from the liver, so Dr. Welch wondered

whether it was coming from the pancreas. It was not until after he had freed most of the attachments that it became clear that it had arisen on the diaphragm. In the attempt to dissect it from the diaphragm, the cyst was entered.

DR. EDGAR B. TAFT: The cyst, which was approximately 15 cm. in diameter, had been opened in the operating room as Dr. Ellis has said (Fig. 2). It was surrounded by dense, fibrous and fatty tissue, a large mass of which came from the neighborhood of the kidney. Dr. Welch told me that the cyst was inadvertently opened in the attempt to free it from the diaphragm. After evacuating some of the contents from the cyst, he removed it, leaving a piece of ectocyst wall attached to the diaphragm because he would have had to sacrifice a portion of the diaphragm to remove it. He was sure that no daughter cysts had been left in the peritoneal cavity.

The cyst wall, with many small daughter cysts inside, is characteristic of echinococcal cysts. Microscopically, these are often disappointing. They show only a tremendous amount of necrotic débris and chitinous material within the cyst. Around the cyst was dense, fibrous tissue with a few inflammatory cells and some giant cells, which contained chitin from the parasites. I did not find typical hooklets in the sections, but the rest of the picture was entirely characteristic of this lesion.

The patient recovered very well, although he still has a small, draining sinus. Dr. Welch had been in communication with Dr. Rodolfo E. Herrera, whom many of you may remember and who was this man's physician in Guatemala. Dr. Herrera said that the patient could not have acquired that disease in Guatemala because there is no echinococcal disease there; however, he was born in Spain, where the disease is endemic.

DR. J. T. HEYL: Is it not true that the larger the size of the cyst, the less the likelihood of scoleces?

DR. TAFT: I have seen scoleces just once. I did not know that they were commonly seen. Usually, by the time the cyst becomes this large they may be quite degenerated, and such anatomical details are not often preserved.

DR. HEYL: Is it not unusual to have echinococcal cysts of this size without any calcification?

DR. TAFT: Calcification is the rule, from what I have read.

DR. QUINBY: This is the second large solitary echinococcal cyst discovered this year in this hospital. Stimulated by the other patient, I looked them up and found that we had 12 in the past twenty years. Most of our patients showed multiple foci of disease, and about a third had persistent or recurrent disease since they had had previous operations.

The literature on the subject shows that there are two forms of the disease. One is the hydatid cyst, as in this patient, caused by the *Echinococcus granulosus*. It may involve liver, lungs, kidney and peritoneum and may be solitary or may have many cysts. Patients with pulmonary involvement may cough up daughter cysts or effect a spontaneous cure by coughing up the entire cyst. There is one famous patient, remembered by our older surgeons, who had common-duct obstruction from a daughter cyst. Another more recent one had wide distribution, with involvement of bone, and cysts have been passed per urethra.[1] The other form of the disease, which is quite rare, is the alveolar form that invades organs as an expanding network of alveoli without the chitinous outer wall. It is called *E. multilocularis*, and there is reasonable evidence that it is a separate species and not merely a variant of the granulosus type.[2-4]

Rodents may be intermediate hosts for both forms. The carnivorous animals, such as wolves, foxes, coyotes and dogs, harbor the adult worm, which they acquire by eating the infected organs of herbivorous animals, such as moose, deer, caribou and sheep. Other herbivores then eat grass infected with the excreta of carnivores. Man is infected usually through vegetables or contact with infected dogs.[1]

Rausch has studied the disease in Alaska[2,3] and I understand that Dr. William Shorey, formerly of our surgical service, is deeply interested in this disease as a result of his stay in Beirut. The National Institutes of Health are currently concerned with the disease, and Dr. Chia-tung Pan, at the Harvard School of Public Health, also has had much experience with it.

DR. TAFT: Do you have any data on the presence of calcification in the cysts?

DR. QUINBY: In our series the large cysts that had been operated upon only once often showed a ring of calcium. Other less characteristic calcifications in the liver were frequently seen. Small lesions showed little or no calcification. Although calcification may be a function of size, I believe it also reflects maturity. The cysts may remain static, rupture, become infected or burn out. Calcification of the cyst wall does not guarantee death of the cyst, as shown by our other patient this year, who had myriads of scoleces in the fluid and a clear ring of calcium in the x-ray films.

The technical difficulties in removing the cyst without spillage and the tendency to multiple areas of cyst development render the disease difficult to cure.

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The New England Journal of Medicine

Official Organ of
THE MASSACHUSETTS MEDICAL SOCIETY

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A MORTAL ANTIPATHY

THE approaching centennial of that otherwise timeless periodical, the *Atlantic Monthly*, calls to mind its indebtedness, of a sort, to Boston medicine in respect both to its accouchement and to its early care and training. For when, in 1857, the publishing firm of Phillips, Sampson and Company, in Winter Street, Boston, proposed to James Russell Lowell that he assume the editorship of a new and nameless magazine, that rising young essayist accepted only on condition that Dr. Oliver Wendell Holmes be engaged as the first contributor.

As it turned out the credit eventually went to Holmes, not only for having suggested the name for the new publication but for having assured its early success as well. If Lowell lighted the fuse that fired the magazine it was Holmes, with his creation of that conversational addict, the Autocrat of the Breakfast Table, who supplied the powder that sent it rocketing.

Dr. Holmes, although a medical anomaly in 1857, being a physician who did not practice his profession — a minister without portfolio, so to speak — was nevertheless by way of becoming the Massachusetts Medical Society's most distinguished fellow. He had already occupied the chair of anatomy at the Harvard Medical School for ten years, and one at least of his medical essays — "The Contagiousness of Puerperal Fever," published in 1843 (although not in the *Boston Medical and Surgical Journal*) — had become a classic of its kind. Even if his growing reputation was as a poet, essayist, lecturer and wit, Holmes nevertheless was at that time and always has been the doctor; as much so as any in the profession whose steps have taken them so far afield.

Holmes's claim to this active position in the ranks of his fellows rests in part on his professorship, which he held for thirty-five years, but more especially on his continued devotion to the affairs of medicine and of the Massachusetts Medical Society. This position made especially appropriate his election as orator in 1860, when he delivered the famed discourse on "Currents and Counter-Currents in Medical Science," although he never became an officer of the Society. His lack of official participation on such a stage is more than offset by his election, better suited to one who was earning his living by the pen, as the first president of the Boston Medical Library.

If those who experience a natural reluctance to preside over a meeting or to indulge in a public debate are downcast by their apparent failing in this particular, they may find some comfort in Dr. Holmes's own words on the subject. "I am slow in apprehending parliamentary rules and usages, averse to the business details many persons revel in," he admitted, "and I am not in love with most of the actively stirring people whom one is apt to meet in all associations for doing good."

This mortal antipathy is further revealed in other excerpts from the chapter fittingly headed "The Doc-

tor's Distaste for Public Affairs" in the *Life and Letters.** "I hate the calling of meetings to order," he confessed, and it is possible that there are those of the Society's present fellowship who might agree with him. "I hate the nomination of officers, always fearing lest I should be appointed Secretary. I hate being placed on committees. They are always having meetings at which half are absent and the rest late." He entertained a prejudice even against "being officially and necessarily in the presence of men most of whom, either from excessive zeal in the good cause or from constitutional obtuseness, are incapable of being *bored*. . . ."

And so the good doctor trod his wayward if singularly productive path, his daily bread unleavened by the fermentation implicit in parliamentary debate or the less spectacular colloquies inherent in the meetings of committees.

*Morse, J. T., Jr. *Life and Letters of Oliver Wendell Holmes.* Vol. 1. 358 pp. Boston and New York: Houghton, Mifflin and Company, 1896.

THE GRACES OF THE SPIRIT

THE concern expressed by the writer of the letter, "Medical Ethics in the Atomic Age," printed elsewhere in this issue of the *Journal,* is widely shared by many thoughtful physicians. In his communication a novel suggestion is proposed.

Although the modern climate of economic and statistical measurement used in medical research has been immensely stimulating, it has all but stifled the older standards of professional behavior. This, the author believes, is not because this modern climate is inimical to ethical considerations, but because the medical profession has neglected to apply these same economic, statistical and research technics and resources to its ethical concepts. Were this to be done, he hopes, what now seems to have been outdated might revive and flourish in conformity with the present practice of medicine.

If one believes that a code of ethics can create new professional standards he must also believe that a good Sunday sermon can create a new standard of weekday behavior. The ethic, and the sermon too, can undoubtedly shape and mold an inborn, or previously existent, capacity to behave, but these things are then expressions of the previously existing capacities, and are more analogous to the Common Law, calling for its obedience or enforcement. They are statements of what have already been accepted, in the best interests of society, and are recognized as rules of good conduct.

Concern for the preservation or improvement of practical ethical behavior a few years ago led to the passing of a resolution, by the Council of the Massachusetts Medical Society, that the medical schools in Massachusetts be requested to give instruction in this matter. This was presumably being done anyway, but how effectively such instruction can be imparted again must depend upon the capacity of the congregation to absorb as well as the diligence of the high priests to expound. How, one wonders, does a school of divinity select receptive students and inculcate in them the graces of the Spirit? Have they ever considered the application of economic and statistical yardsticks to their output, or have they embarked upon research programs to counteract the untoward effects of research (if such there are) upon the attitudes and the graces of mankind?

The proposal put forward by Colonel Glascock is fundamentally homeopathic; the symptoms are to be removed by applying the influences that allegedly brought them about. In it there could well be the same homeopathic kernel of truth, and none can deny that honest homeopathy has done much good in the world.

CENTENARIAN

MEDICAL journals have come and gone to the numbers of no one knows how many thousands since *Zodiacus-Medico-Gallicus* crossed the barricades and appeared in Paris in 1679. According to a recent estimate resulting from a study made by the Welch Medical Library of Johns Hopkins University, no less than three quarters of a million "useful" scientific papers were published in 1948 in 15,000 "useful" scientific journals. The remaining 20,000 scientific periodicals contained mostly matter of less importance!

Included in this host of publications were 4454 "substantive" (that is, substantial) and 1626 nonsubstantive medical serials; of this total number 1108 are general or all-purpose journals more or less covering the entire field of medicine.

An increasing number of the periodicals in current publication have passed the century mark in still viable condition, having survived war and pestilence and famine, and to the list the *Journal* now welcomes the *Nederlandsch Tijdschrift voor Geneeskunde* of Amsterdam, which celebrates its centennial on January 4 and 5, 1957, under the present editorship of Professor Dr. J. R. Prakken.

AUXILIARY MEANS ASSIST

PHILOSOPHERS, poets, playwrights and wisecrackers — not to overlook males whose only concern is that of being good fathers, brothers, or husbands — have over the ages had so much to say about the wiles, whims and character of women that the women themselves, having obtained the equal recognition for which they so valiantly fought, now toss off all unfavorable witticisms and criticisms fostered and broadcast by the possibly insecure male with a demonstrative shrug of the shoulders, indicating an equanimity that comes from knowledge of their essential role in the scheme of things.

The Woman's Auxiliary to the Massachusetts Medical Society, being composed, obviously, of women, underwent at its inception back in 1947 the same sort of male-sponsored witticisms and criticisms to which the female has so long been heir. Many of them persist even to this day. Many will continue *ad infinitum*, for such is the nature of masculine profundity.

But the shoulders of the women of the Auxiliary (figuratively speaking) are broad. They have borne the brunts well, and what is more important, these helpmeets have borne well the duties incumbent on a medical auxiliary.

The Woman's Auxiliary to the Massachusetts Medical Society, in its work ranging from legislative activities and nurse recruitment to health education and cultivation of friendly relations among physicians' families, has earned a permanence in organized medicine.

A deep debt of gratitude to the Auxiliary is cheerfully acknowledged for its wholehearted support of the Society's aims and projects — and for its devoted "assist."

Dissecting Material. — *A Paragraph in the* New York Times *states that in Boston, Philadelphia and Baltimore there is a scarcity of subjects. The* Times *says, "this is always a difficulty in the* provincial *towns." We have no objection to being called provincial in such good company, but we can assure the* Times *that the want to which it alludes has not existed in Boston.*

Boston M. & S. J. *January 1, 1857*

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Spontaneous Rupture of the Uterus

A thirty-six-year-old gravida 3, para 2, was admitted to the hospital in early active labor with intact membranes, apparently four weeks postmature by dates. Previous pregnancies and the current prenatal course had been absolutely normal. Admitted at about 8 p.m. with the presenting part above the spines, she began to have strong labor about midnight, when she received sedation and the cervix was found to be dilated 3 cm.; the presenting part had descended to the mid-pelvis. The position of the presenting part was indistinct in this station, but the patient and fetus were in good condition and the labor continued normally, with examinations by her physician at frequent intervals. The last examination was at 3:10 a.m., the cervix now being found dilated 4 cm. The position was described as left occiput anterior, the station as "high mid-pelvic," contractions as recurring at three-minute intervals, and the patient as satisfactorily medicated. Twenty minutes later, she suddenly collapsed and died despite the usual emergency measures. No pituitary extract or other oxytocic had been given at any time. The pelvis was of ample size, the patient having had 2 babies weighing about 3.4 kg. (7½ pounds) each.

At autopsy the trunk of a fetus weighing 2.7 kg. (6 pounds) and a large volume of blood were found to fill the peritoneal cavity. These had escaped through a laceration of the lower uterine segment on the right that extended through the broad ligament. The head was discovered to be engaged in a posterior face presentation, and microscopical examination of the myometrium of the lower segment at the site of rupture showed focal necrosis of the muscle in contrast to intact fibers elsewhere in the uterus. The pathologist pointed out, "Since several hours must elapse during life before necrosis of cells becomes evident histologically, we have microscopical evidence here that the lower uterine segment had undergone necrosis before rupture."

This was classified as a nonpreventable death due to spontaneous rupture of the uterus intrapartum caused by a posterior face presentation. Careful interpretation of the gross findings at autopsy leaves little doubt that the malpresentation was directly responsible for uterine rupture and that this presentation and position must have been a left posterior face high in the pelvis, not yet rotated. During the short period between the onset of labor and death it seems hardly reasonable to have expected the obstetrician to have diagnosed this unlikely malpresentation. Even if, with good fortune and unusual acumen, the diagnosis had been made, however, it would have been considered inexcusable in most obstetric institutions to have done anything other than to allow normal labor to continue in the hope of spontaneous rotation or with the possibility of manual flexion to the vertex after full dilatation. Thus, since apparently normal labor did continue without interference but was followed by spontaneous, sudden uterine rupture without warning, we are at a loss to offer any suggestions in retrospect that might help to avoid such a tragedy in the future.

John Figgis Jewett, M.D.
Chairman

CORRESPONDENCE

MEDICAL ETHICS IN THE ATOMIC AGE*

To the Editor: The increasing tempo of change affects all aspects of modern culture; this is especially true of the technics and practices of the medical profession. The rapidity of change in medical ethics in particular calls for an earnest inquiry into the virtue of the pattern of behavior we are advocating for ourselves, as well as for the physicians and surgeons of the future. Let us therefore devote an appropriate amount of money and trained manpower to the study of ethics, in relation to patient care, comparable to the resources we are expending upon research in scientific and technical fields. Whereas new ethical codes are not as conspicuous as new discoveries, the ultimate effect of such a study might have tremendous impact. Emphasis upon the unwritten rules under which these discoveries are applied to patients' needs is of equal importance with that being placed upon other forms of medical research.

In the writings of eminent contemporary philosophers and historians, modern man is characterized as becoming overly concerned with "economics." Physicians are no exception. Our actions are directed according to the broad financial or statistical situation. Individual problems must be made to conform to percentages, averages or norms. In fact, a new language and a new science of economics and statistics has been devised to speed man upon the road to the "practical" approach to the solution of various problems. Time for the study of exceptions is indeed limited. Success, in an arbitrary majority of cases, is considered to be very praiseworthy, but little attention is given to the patients in whom a given pattern of therapy has failed to have the desired results.

The medical profession is contributing its full share to this so-called scientific progress. Are we certain, however, that this tendency is best for either physician or patient?

Much discussion is given to the importance of interpersonal relations between the family physician and his patients. We remember the visits we used to make to the homes of our patients in order to learn more about them. Not only are the family physicians disappearing but also home visits and night calls are becoming less frequent. What is the reason for this decline in personal attention? Stated bluntly, the reason is an economic one. The physician can see more patients in his office. His income is such that he does not have to respond to night calls. Only the less financially secure, modern practitioners, and those who adhere to the former ethical standards, respond to telephone calls outside office hours.

Another well recognized ethical trend based upon economic considerations is that of fee splitting. All of us deplore this development. What is being done to study the ethics of this practice and to discover more acceptable means of assisting the referring physician to choose the best qualified specialist for his patient's condition? Experience has shown that this economic problem requires an economic solution. Ethical preaching will not eliminate its evil.

The prospect of masses of casualties in the event of war is deceiving some of our medical planners to the extent that they openly advocate the denial of medical and surgical care to casualties with little chance of survival. They take the position that time and available medical resources will not permit such patients to be given professional attention, since it is not believed to be statistically profitable. This position is diametrically opposed to the time-honored ethical concept that while there is life there is hope, and that we, as physicians, must offer our services as long as there is the slightest hope. Research on this point might bring forth a solution. Let us not sacrifice our ethical standards until it has been conclusively proved that there is no alternative.

Because of economic influences a few physicians are voluntarily repudiating their obligations to render service in support of national defense, either as civilians or as members of the armed forces. They believe themselves to be too busy to participate in civil-defense planning and organization. They must be drafted into the armed forces under a special act of Congress. However, ethical consideration requires that their services not be limited to the care of the infirm, but that they recognize their full obligation to society, which has made possible their medical education and their position among the citizens who are responsible for the destiny of the nation. Serious inquiry into this regrettable situation may be productive of a means by which physicians can fully discharge this ethical obligation without economic pressure.

A major portion of the esteem in which our profession is held by the lay population is based upon its former ethical standards. If we sacrifice these standards to economic considerations and statistical analyses we become "technicians" and will no longer be worthy of our honored position in society.

COLONEL HAROLD W. GLASCOCK, JR., M.C.
APO 227, United States Army

*The opinions expressed herein are those of the author and not necessarily those of the Department of the Army or any agency thereof.

BOOK REVIEWS

Atlas und Praktikum der Dermatologie und Venerologie. By Professor Dr. med. W. Burckhardt, Zürich. 4°, cloth, 279 pp., with 164 illustrations. Berlin: Urban and Schwarzenberg, 1955. DM. 48.- $12.00.

It is the author's purpose to provide the general practitioner, the specialist of other specialties than dermatology, the dentist and the student with a nonvoluminous atlas and textbook of dermatology and venereology. Nevertheless, it should enable the physician to acquaint himself with the fundamentals of diagnosis and therapy of all common and some rare dermatoses as well as venereal diseases.

The symptomatology, etiology, and histology of the various disorders are well described. The reviewer cannot agree with the author's grouping of lichen nitidus with lichen ruber and listing of parapsoriasis guttata, parapsoriasis lichenoides and pityriasis rubra pilaris as diseases related to psoriasis. Concerning the therapeutic part of the text, too many medications are listed in the various chapters, making it difficult for the beginner to choose the proper treatment. The frequent recommendation of ointments containing local anesthetics, antihistamines, sulfonamides and penicillin is not in line with current dermatologic therapy. The author's statement that x-ray therapy is the best treatment of skin carcinoma will not meet with general approval. The 65 black and white and 99 colored illustrations are excellent and represent the main attraction of Burckhardt's publication. Even the physician not familiar with the German language will benefit greatly from the study of this reasonably priced atlas of well chosen clinical pictures covering the entire array of skin and venereal diseases.

ALFRED HOLLANDER, M.D.

Understanding and Counseling the Alcoholic: Through religion and psychology. By Howard J. Clinebell, Jr. 8°, cloth, 252 pp. New York: Abingdon Press, 1956. $3.75.

More people than the doctor and his assistants have to cope with the alcoholic patient. As often as not, this problem falls on the family lawyer or the minister, as the case may be. Sometimes, the heavy burden rests with the wife or with friends. Friends often give good psychotherapy. This has been proved true of the most friendly of all groups, Alcoholics Anonymous.

Here is a book based on considerable personal experience and much study of the problem, written by a minister of the Gospel, who has taken time out from his busy clerical work to include two periods of study, one at the William Alanson White Institute of Psychiatry in New York (1948-1951), where Dr. Clinebell received a certificate in applied psychiatry for ministers, and the other at the Yale Summer School of Alcohol Studies given at Fort Worth, Texas in 1949. Although the motive in this case is spiritual, his attitude is strongly that of the clinician.

This book is plainly written and easily read, and although the religious approach is emphasized, in its own way makes a fresh approach to the understanding of the problem of al-

coholism. The references are excellent, and the index is complete. The publication of this volume marks another milestone in the secular program of the study and treatment of problem drinkers.

MERRILL MOORE, M.D.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Operative Surgery. Edited by Charles Rob, M.C., M.Chir., F.R.C.S., professor of surgery, St. Mary's Hospital, London; and Rodney Smith, M.S., F.R.C.S., surgeon, St. George's Hospital, London. 4°, cloth, 347 pp., with illustrations. London: Butterworth and Company, Limited, 1956. (Distributed in the United States by F. A. Davis Company, Philadelphia.)

Diabetes Mellitus: Handbook for physicians. By Howard F. Root, M.D., Sc.D., medical director, Joslin Clinic, Boston, lecturer in medicine, Harvard Medical School, and vice-president, International Diabetes Federation; and Priscilla White, M.D., Sc.D., Joslin Clinic, Boston, instructor in pediatrics, Tufts University School of Medicine, and physician, New England Deaconess and Boston Lying-in hospitals. 8°, cloth, 346 pp., with 33 tables and 6 charts. New York: Landsberger Medical Books, Incorporated, 1956. $7.00. (Distributed solely by the Blakiston Division of the McGraw-Hill Book Company, New York City.)

Atlas Cerebri Humani: The inner structure of the brain. By E. Ludwig and J. Klingler, Anatomisches Institut der Universität Basel. F°, cloth, 136 pp., with 100 illustrations. Boston: Little, Brown and Company, 1956. $18.50. (Written in English, German, French and Spanish.)

Functions of Autonomic Transmitters. By J. Harold Burn, M.D., professor of pharmacology, Oxford University, England. 8°, cloth, 228 pp., with 43 illustrations and 37 tables. Baltimore: The Williams and Wilkins Company, 1956. $5.00. (*The Abraham Flexner Lectures, Series,* No. 13.)

Community Organization: Action and inaction. By Floyd Hunter, Ruth Connor Schaffer and Cecil G. Sheps. 8°, cloth, 268 pp. Chapel Hill: University of North Carolina Press, 1956. $5.00. (Published for the Institute for Research in Social Science.)

NOTICES

BOSTON GASTROENTEROLOGICAL SOCIETY

A dinner meeting of the Boston Gastroenterological Society will be held at the Hotel Vendome, on Wednesday, January 9, at 6:30 p.m. The panel discussion will be on "Diseases of the Pancreas."

PROGRAM

Cancer of the Pancreas. Charles G. Child, III., M.D.

Acute Pancreatitis. Perry J. Culver, M.D.

Laboratory Aids in the Diagnosis of Pancreatic Disease. Franz J. Ingelfinger, M.D.

Surgery of the Sequelae of Pancreatitis. Kenneth Warren, M.D.

Members and guests will be included in the meeting.

BENJAMIN WATERHOUSE MEDICAL HISTORY SOCIETY

A meeting of the Benjamin Waterhouse Medical History Society will be held in the Evans Amphitheater, Massachusetts Memorial Hospitals, on Monday, January 21, at 7:30 p.m.

Dr. Charles W. Robertson will talk on "Medical Illnesses of our Presidents."

All interested physicians are invited to attend.

NEW ENGLAND CARDIOVASCULAR SOCIETY

A meeting of the New England Cardiovascular Society will be presented by the Massachusetts Memorial Hospitals, with invited papers from New England, in the Morse Auditorium, Museum of Science, Science Park, Boston, on Monday, January 14, at 8 p.m.

PROGRAM

Massachusetts Memorial Hospitals, Robert W. Wilkins, M.D., presiding:

A Self-Adjusting Hydrostatic Stocking for the Treatment of Chronic Venous Stasis. J. E. Wood, M.D.

Sodium and Water Metabolism in Arterial Hypertension. W. Hollander, M.D., A. Chobanian, M.D., and B. A. Burrows, M.D.

Upright QRS Complexes in $V4_R$. G. H. Whipple, M.D., and J. D. Coffman, M.D.

Chemical Changes in the Blood and Control of Cardiac Output. W. E. Huckabee, M.D.

Invited Papers from New England, Lewis Dexter, M.D., presiding:

Chest Pain with Inverted Precordial T-Waves as the Only Electrocardiographic Abnormality. Frank B. Cutts, M.D., Frank Merlino, M.D., and Frederick W. Easton, III., M.D.

Comments on the Course of Coronary Disease in the Country. Franklin K. Paddock, M.D., Thomas C. Clifford, M.D., and Henry J. Wheelwright, M.D.

Prognostic Factors in Coronary Heart Disease with Particular Reference to the "Psyche." Samuel J. King, M.D.

Resection of the Anginal Pathway. Clem F. Burnett, Jr., M.D., and James A. Evans, M.D.

Free parking privileges are available on the premises at Science Park (emergency telephone number, RIchmond 2-1410).

Interested physicians and medical students are cordially invited to attend.

SOCIETY MEETINGS AND CONFERENCES

JANUARY 9. Boston Gastroenterological Society. Notice above.
JANUARY 14. New England Cardiovascular Society. Notice above.
JANUARY 16–19. International Fertility Association. Page 1109, issue of December 6.
JANUARY 17. Arthritis Study Unit. Page 831, issue of October 25.
JANUARY 21. Benjamin Waterhouse Medical History Society. Notice above.
FEBRUARY and APRIL. Massachusetts Society for Research in Psychiatry. Page 56, issue of July 5.
FEBRUARY 4. Yale University School of Medicine. Page 1163, issue of December 13.
FEBRUARY 23 and 24. Los Angeles Radiological Society. Page 1163, issue of December 13.
MARCH 4–7. College of General Practice of Canada. Page 1205, issue of December 20.
MARCH 7–9. Symposium on Fundamental Cancer Research. Page 1205, issue of December 20.
APRIL 27. Postgraduate Medical Institute. Page 785, issue of October 18.

CALENDAR FOR THE WEEK BEGINNING THURSDAY, JANUARY 3

THURSDAY, JANUARY 3
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Surgical Grand Rounds. Dr. John Spellman and staff. Saint Elizabeth's Hospital.

8:00–9:00 a.m. Medical Journal Club. Joslin Auditorium, New England Deaconess Hospital.
*8:45–9:45 a.m. Cardiac Grand Rounds. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*9:00 a.m. Neurological Rounds. Dr. Kane. Evans 2 Conference Room, Massachusetts Memorial Hospitals.
*9:00–10:00 a.m. Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.
*10:00–11:00 a.m. Combined Medical-Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.
*10:15 a.m.–12:00 m. Medical Grand Rounds. Dr. Keefer. Evans 8 Amphitheater, Massachusetts Memorial Hospitals.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Medical Grand Rounds. Dr. Sylvester McGinn and staff. Saint Elizabeth's Hospital.
*11:00 a.m.–12:00 m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*12:00 m. Clinicopathological Conference. Dr. Benjamin Castleman and associates. Pathology Amphitheater, Massachusetts General Hospital.
*12:00 m.–1:00 p.m. Surgical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*12:15–1:15 p.m. Tumor Clinic. Dr. T. W. Botsford. Amphitheater, Peter Bent Brigham Hospital.
*3:00 p.m. Thoracic Conference. Aortic Stenosis and Aortic Insufficiency. Dr. Dwight E. Harken. Main Amphitheater, Peter Bent Brigham Hospital.
*3:30 p.m. Gastroenterology Conference. Dr. Ingelfinger. Massachusetts Memorial Hospitals.

FRIDAY, JANUARY 4
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
*10:00 a.m. Ward Rounds. Massachusetts Memorial Hospitals.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:30 p.m. Medical Grand Rounds. Stearns Auditorium, New England Center Hospital.
*11:30 a.m. Tumor Clinic. Drs. Soutter and Lemon. Robinson 4, Massachusetts Memorial Hospitals.
*12:00 m. Pediatric Grand Rounds. Thorndike Amphitheater, Boston City Hospital.
*12:30–1:30 p.m. Surgical Grand Rounds. Stearns Auditorium, New England Center Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*2:00–3:00 p.m. Pathology Conference. Dr. James Graham. Saint Elizabeth's Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Morton Street, Jamaica Plain.
*4:30 p.m. Neuroradiologic Conference. X-Ray Conference Room, New England Deaconess Hospital.

SATURDAY, JANUARY 5
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium. New England Deaconess Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*8:30–10:00 a.m. Surgical Grand Rounds. Drs. Charles G. Child, III, and A. J. A. Campbell and staff. First (Tufts) Surgical Service, New Cheever Amphitheater, Dowling Building, Boston City Hospital.
*9:00–10:00 a.m. Anesthesiology Conference. Dr. Benjamin Etsten. Anesthesia Laboratory, New England Center Hospital.
*9:30–11:00 a.m. Surgical House Officers' Conference. Second-Floor Conference Room, Carney Hospital, Dorchester.
*9:30 a.m.–12:00 m. Grand Rounds. Haynes Memorial Hospital, Brookline.
*10:00 a.m. Ward Rounds. Massachusetts Memorial Hospitals.
*10:30 a.m. Teaching Ward Rounds. Ward South 2, Free Hospital for Women.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Hematology Conference. Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.

MONDAY, JANUARY 7
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*10:00 a.m. Ward Rounds. Massachusetts Memorial Hospitals.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:30 p.m. Staff Conference. Child Psychiatry. By appointment. Conference Room (Burnham 7), Massachusetts General Hospital.
*12:00 m.–1:00 p.m. Pediatric Clinicopathological Conference. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*12:00 m.–1:00 p.m. Staff Meeting. Obstetrical and Gynecological. Drs. Abrams and Parker. Evans 8 Amphitheater, Massachusetts Memorial Hospitals.
*12:00 m.–1:00 p.m. Metabolism Conference. Dr. Schwartz. Stearns Auditorium, New England Center Hospital.
*12:00 m.–1:00 p.m. Tumor Conference. Dr. C. C. Lund and members of the Tumor Board. Dowling Amphitheater, Boston City Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*2:00–3:00 p.m. X-Ray Conference. Dr. William Carey. Saint Elizabeth's Hospital.
*3:00–4:00 p.m. Neuroradiologic Conference. Dr. Bertram Selverstone. Stearns Auditorium, New England Center Hospital.
*4:00–5:30 p.m. Anesthesiology Conference. Dr. Benjamin Etsten. Stearns Auditorium, New England Center Hospital.
*4:00–5:30 p.m. Anesthesiology Conference. Anesthetic Practice in South Africa. Dr. J. W. Mostert. Surgical Conference Room, Peter Bent Brigham Hospital.
*5:00–6:30 p.m. Anesthesiology Group of the Lahey Clinic. Joslin Auditorium, New England Deaconess Hospital.
*7:00–9:00 p.m. Slide Seminar in Pathology. Dr. Edward T. MacMahon. Stearns Auditorium, New England Center Hospital.
*7:00–9:00 p.m. Anesthesia Teaching Conference of Greater Boston. (A) Pharmacology of Muscle Relaxants. (B) Clinical Use of Muscle Relaxants. Dr. Arrowood. Auditorium, Jimmy Fund Building, Children's Medical Center, 35 Binney Street.

TUESDAY, JANUARY 8
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical Grand Rounds. Pathology Conference Room, Carney Hospital, Dorchester.
*10:30 a.m. Medical Grand Rounds. Main Conference Room (Ground Floor), Lemuel Shattuck Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m.–1:00 p.m. Pediatric Grand Rounds. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
*12:00 m.–1:00 Cardiac Conference. Drs. Magendantz and Selverstone. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. X-Ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Medical Pathological Conference. Massachusetts Memorial Hospitals.
*2:00–3:00 p.m. Hematology Conference. Dr. Mario Stefanini. Saint Elizabeth's Hospital.
*2:00–3:00 p.m. Surgical Pathological Conference. Dr. Sheldon C. Sommers. Evans 8 Amphitheater, Massachusetts Memorial Hospitals.
*5:00 p.m. Surgical Journal Review. Mount Auburn Hospital, Cambridge.
*5:00–6:00 p.m. Service Meeting Followed by Clinical Conference (Medical, Surgical, Obstetric). Faulkner Hospital.

WEDNESDAY, JANUARY 9
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Problems. Deaconess II, New England Deaconess Hospital.
*8:00–9:00 a.m. Surgical Grand Rounds. Auditorium, Carney Hospital, Dorchester.
*9:00–10:00 a.m. Surgical Grand Rounds. Dr. Smithwick. Evans 8 Amphitheater, Massachusetts Memorial Hospitals.
*10:00 a.m. Ward Rounds. Massachusetts Memorial Hospitals.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
11:00 a.m. Orthopedic Grand Rounds. Bigelow Amphitheater, White 3A, Massachusetts General Hospital.
*11:00 a.m.–12:00 m. Pediatric Conference for Practitioners. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*12:00 m.–1:00 p.m. Boston State Hospital Psychiatry Seminar. Reception Building Auditorium, 591 Morton Street, Dorchester.
*12:00 m.–1:00 p.m. Roentgen Diagnostic Conference. 5th-floor teaching unit, Beth Israel Hospital.
*12:00 m.–1:00 p.m. Neurology, Neurosurgery and Psychiatry Conference. Drs. John F. Sullivan, Justin Hope and Bertram Selverstone. Stearns Auditorium, New England Center Hospital.
*12:00 m.–1:00 p.m. Pediatric Medical-Surgical Rounds. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*12:00 m.–1:00 p.m. Pediatric Clinicopathological Conference. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*12:15 p.m. Vascular Rounds. Drs. Edward A. Edwards and Chilton Crane. D-Main, Peter Bent Brigham Hospital.
*12:30–1:30 p.m. Weekly Staff Review of Autopsies. Dr. William A. Meissner. Joslin Auditorium, New England Deaconess Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*1:00 p.m. Massachusetts General Hospital Hand Clinic. The Clinics of the Massachusetts General Hospital.
*1:00–2:00 p.m. Surgical Staff Meeting. Dr. Smithwick. Evans Conference Room, Massachusetts Memorial Hospitals.
*2:00 p.m. Rectal Clinic. Peter Bent Brigham Hospital.
*2:00 p.m. Vascular Rounds. Robinson 4, Massachusetts Memorial Hospitals.
*2:00–3:00 p.m. Pediatric Conference for Practitioners. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*4:00–5:30 p.m. Fracture Lecture. Boston City Hospital.
*4:00–6:00 p.m. Overholt Thoracic Conference. Joslin Auditorium, New England Deaconess Hospital.
*6:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*6:30 p.m. Lahey Clinic Lectures. Panel Discussion — Peripheral Vascular Disease. Dr. James A. Evans, Moderator. Drs. Cornelius E. Sedgwick, Carl C. Bartels, David P. Boyd and Ferdinand A. Salzman. Joslin Auditorium, New England Deaconess Hospital.

*Open to the medical profession.